In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: October 31, 2024

MARIANNE SIMENETA,	*	PUBLISHED
Petitioner,	*	No. 18-859V
v.	*	Special Master Nora Beth Dorsey
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Ruling on Entitlement; Pneumococcal Conjugate ("Prevnar 13") Vaccine; Guillain-Barré Syndrome ("GBS").
Respondent.	*	

Michael Andrew London, Douglas & London, P.C., New York, NY, for Petitioner.
James Vincent Lopez, U.S. Department of Justice, Washington, DC, for Respondent.

RULING ON ENTITLEMENT[1]

On June 18, 2018, Marianne Simeneta ("Petitioner"), filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2018),[2] alleging that as a result of a pneumococcal conjugate vaccine ("Prevnar 13") administered on August 1, 2015, she developed Guillain-Barré Syndrome ("GBS"). Petition at Preamble, ¶¶ 2, 4 (ECF No. 1). Respondent argued against compensation, stating "entitlement to compensation must be denied, and the petition dismissed." Respondent's Report ("Resp. Rept.") at 9 (ECF No. 13).

[1] Because this Ruling contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the Ruling will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to -34 (2018) ("Vaccine Act" or "the Act"). All citations in this Ruling to individual sections of the Vaccine Act are to 42 U.S.C.A. § 300aa.

After carefully analyzing and weighing the evidence presented in accordance with the applicable legal standards,[3] the undersigned finds Petitioner has provided preponderant evidence that the Prevnar 13 vaccine she received caused her GBS, satisfying Petitioner's burden of proof under Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, Petitioner is entitled to compensation.

I. ISSUES TO BE DECIDED

Diagnosis is not in dispute. The parties agree that "[t]here is no dispute that Petitioner developed [GBS] in August 2015." Joint Prehearing Submission ("Joint Submission"), filed August 20, 2021, at 2 (ECF No. 72). They also agree that before she received her Prevnar 13 vaccine, "Petitioner did not exhibit any neurological symptoms and did not carry a diagnosis of a neurological or autoimmune condition." Id. at 1.

The parties dispute a factual issue: "[w]hether the symptoms Petitioner was treated for on August 15, 2015 by Patricia[] Corcoran, N.P., were allergic in nature or consistent with an upper respiratory infection [("URI")]." Joint Submission at 2.

Further, the parties dispute causation and all three Althen prongs: (1) whether Petitioner presented preponderant evidence that the Prevnar 13 vaccine can cause GBS (Althen prong one), (2) whether Petitioner presented preponderant evidence of a logical sequence of cause and effect that the Prevnar 13 vaccine did cause Petitioner's GBS (Althen prong two), and (3) whether Petitioner presented preponderant evidence that the onset of symptoms fits the medically-accepted time frame and is therefore medically-appropriate (Althen prong three). Joint Submission at 2.

II. BACKGROUND

A. Procedural History

Petitioner filed her petition on June 18, 2018 followed by medical records.[4] Petition; Petitioner's Exhibits ("Pet. Exs.") 1-7. On April 1, 2019, Respondent filed his Rule 4(c) Report, arguing against compensation. Resp. Rept. at 9.

[3] While the undersigned has reviewed all of the information filed in this case, only those filings and records that are most relevant will be discussed. See Moriarty v. Sec'y of Health & Hum. Servs., 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.") (citation omitted); see also Paterek v. Sec'y of Health & Hum. Servs., 527 F. App'x 875, 884 (Fed. Cir. 2013) ("Finding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.").

[4] Medical records were filed throughout litigation.

Thereafter, Petitioner filed an expert report from Dr. Salvatore Q. Napoli in August 2019 and Respondent filed expert reports from Dr. Kenneth H. Fife and Dr. Robert T. Naismith in November 2019. Pet. Ex. 8; Resp. Exs. A, C. In 2020, the parties filed supplemental expert reports from Dr. Napoli and Dr. Naismith. Pet. Ex. 20; Resp. Ex. G.

An entitlement hearing was held on September 21 and 22, 2021. Order dated Sept. 22, 2021 (ECF No. 78). Dr. Napoli, Dr. Naismith, and Dr. Fife testified. Transcript ("Tr.") 3, 250. Following the entitlement hearing, the parties requested to file post-hearing expert reports on an issue that arose during the hearing. Joint Status Rept., filed Nov. 1, 2021 (ECF No. 86). On February 14, 2022, Petitioner filed an expert report from Dr. Napoli, and Respondent filed an expert report from Dr. Naismith on June 14, 2022. Pet. Ex. 29; Resp. Ex. M.

Following the parties' post-hearing expert reports, the undersigned held a status conference with the parties on July 19, 2022. Order dated July 19, 2022 (ECF No. 99). The undersigned noted that since the entitlement hearing in this matter, new rulings in Prevnar 13/GBS cases had been issued, including one from the undersigned finding a petitioner entitled to compensation. Id. at 1. In light of these new developments, the undersigned expressed the need for the parties to have a full and fair opportunity to present their respective cases. Id. Petitioner requested the opportunity to file a supplement expert report, which the undersigned found appropriate given the recent rulings and new case law. Order dated Aug. 26, 2022 (ECF No. 101).

Petitioner filed expert reports from Dr. Lawrence Steinman and Respondent filed expert reports from Dr. J. Lindsay Whitton from November 2022 to December 2023. Pet. Exs. 32, 62; Resp. Exs. N, P. On February 5, 2024, the parties filed a joint status report indicating the record was complete. Joint Status Rept., filed Feb. 5, 2024 (ECF No. 147).

This matter is now ripe for adjudication.

B. Medical Terminology

GBS is "an autoimmune peripheral demyelinating nervous system syndrome that affects the nerves of the peripheral nervous system." Tr. 18. The nervous system is comprised of "the central nervous system, which involves the optic nerves, brain, cerebellum, spinal cord, and then as the nerves project out of the spinal cord, they become peripheral nerves." Id. The illness usually presents as "distal symmetric weakness or sensory disorder that may slowly or abruptly spread up the legs, and into the arms," depending on the subtype. Id.

The causes of GBS are not known, however, it is generally defined as "an autoimmune process that is triggered by antigenic stimulation, resulting in demyelination and destruction of peripheral nerves." Resp. Ex. E, Tab 3 at 2.[5] GBS is thought to be triggered by infections or

[5] Roger Baxter et al., Lack of Association of Guillain-Barré Syndrome with Vaccinations, 57 Clinical Infectious Diseases 197 (2013). This was also cited as Resp. Ex. F, Tab 3 and Resp. Ex. N, Tab 6.

immunizations. See, e.g., id. at 2-3; Resp. Ex. N, Tab 9 at 2-3;[6] Resp Ex. N, Tab 15 at 1-3;[7] Resp. Ex. N, Tab 19 at 2.[8] Approximately two-thirds of GBS patients report a gastrointestinal or respiratory infection within six weeks of onset. Resp. Ex. N, Tab 19 at 2; see also Resp. Ex. N, Tab 9 at 2. GBS has also been reported after several different vaccinations, including influenza ("flu"), rabies, meningococcal, hepatitis A, hepatitis B, measles-mumps-rubella, tetanus-diphtheria, and more. Resp. Ex. N, Tab 19 at 2.

C. Stipulated Facts

The parties agreed that Petitioner received the Prevnar 13 vaccination on August 1, 2015, at the age of 64. Joint Submission at 1. While her medical history at the time was "significant for hypertension, osteopenia, asthma, and hyperlipidemia, as well as a hysterectomy and carpal tunnel release surgery," the parties agree Petitioner did not have any prior neurological symptoms or have a neurological diagnosis. Id.

D. Summary of Additional Medical Records[9]

In addition to the facts stipulated to by the parties, the following summary provides additional relevant information.

As stipulated, Petitioner received the Prevnar 13 vaccination on August 1, 2015. Joint Submission at 1. Petitioner was 64 years of age. Id.

On August 15, 2015, Petitioner presented to UP UMG Prompt Care/Urgent Care with complaints of sneezing, occasional productive and dry hacky cough, pain in her neck to back the night before (August 14, 2015), feeling like she had a fever although her temperature was 95 to 97, and chills with hands that were ice cold. Pet. Ex. 3 at 1. She was seen by Patricia A. Corcoran, NP. Id. Petitioner stated she felt better the day she received the Prevnar 13 vaccination on August 1. Id. at 4. The following Monday, August 3, 2015, Petitioner developed sneezing and sinus congestion. Id. She performed a sinus rinse, which seemed to help, however, she started feeling "drained with episodes of chills without fever, sweating at night, neck pain with radiation to her upper back[,] as well as feeling as though her 'bronchiole tubes are clogging.'" Id. Petitioner stated that "she [was] just not feeling well and seems more fatigued/malaise." Id.

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[6] Pieter A. van Doorn et al., Clinical Features, Pathogenesis, and Treatment of Guillain-Barré Syndrome, 7 Lancet Neurology 939 (2008).

[7] Bianca van den Berg et al., Guillain-Barré Syndrome: Pathogenesis, Diagnosis, Treatment and Prognosis, 10 Nature Revs. Neurology 469 (2014).

[8] Anil K. Jasti et al., Guillain-Barré Syndrome: Causes, Immunopathogenic Mechanisms and Treatment, 12 Expert Rev. Clinical Immunology 1175 (2016).

[9] Portions of this summary are taken from Respondent's Report and edited by the undersigned to include additional relevant information. See Resp. Rept. at 2-5.

Review of systems documented Petitioner was negative for fever, ear discharge or pain, and sore throat. Pet. Ex. 3 at 4. Review of systems was also negative for "hemoptysis, sputum production, shortness of breath, wheezing[,] and stridor." Id. Physical examination revealed normal temperature (97.4°F). Id. at 5. Petitioner was not in distress, ears were normal with no redness, and rhinorrhea[10] was present but there was "[n]o mucosal edema." Id. at 6. Right and left maxillary sinus tenderness was present. Id. Pulmonary and chest examination was normal, with normal effort and breath sounds and no respiratory distress. Id. Petitioner had no cervical adenopathy.[11] Id.

Chest X-ray showed "[n]o evidence of active cardiopulmonary process." Pet. Ex. 3 at 6. White blood cell ("WBC") count and differential were normal. Id. at 10. Assessment was cough, malaise and fatigue, and sinusitis. Id. at 6. Petitioner was advised to continue taking Mucinex and Tylenol and to continue sinus rinses as needed, and a Zithromax ("Z-Pak")[12] was ordered. Id. at 7.

Petitioner saw her Primary Care Physician ("PCP"), Dr. Robert Price, on August 17, 2015, with complaints of hypertension and "sinus infectio[n]." Pet. Ex. 2 at 31. She reported being seen and diagnosed at Prompt Care, and that she had been given a Z-Pak, and had two days left of the medication. Id. She was "still having body aches and pains, chills," and elevated blood pressure. Id. (emphasis omitted). She reported that she had "been ill for [the] past week with excessive sneezing and coughing." Id. Her back had "been hurting" and it kept her from sleeping well. Id. Dr. Price's physical examination, including musculoskeletal and neurologic components, was unremarkable, except for "cobblestoning[13] of the posterior pharynx" and an elevated blood pressure. Id. at 32. Petitioner's temperature was 98.3°F. Id. Dr. Price diagnosed

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[10] Rhinorrhea is "the free discharge of a thin nasal mucus." Rhinorrhea, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=43766 (last visited Oct. 17, 2024).

[11] Cervical adenopathy, or lymphadenopathy, refers to "enlarged, inflamed, and tender cervical lymph nodes, seen in certain infectious diseases." Cervical Lymphadenopathy, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=87515 (last visited Oct. 17, 2024); Lymphadenopathy, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=28980 (last visited Oct. 17, 2024).

[12] Zithromax (azithromycin) is an "antibiotic . . . that inhibits bacterial protein synthesis, effective against a wide range of gram-positive, gram-negative, and anaerobic bacteria," and is "used in the treatment of mild to moderate infections caused by susceptible organisms." Azithromycin, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=5244 (last visited Oct. 17, 2024).

[13] "Cobblestone throat involves having inflamed tissue in the back of your throat that looks bumpy." Cobblestone Throat, Cleveland Clinic, https://my.clevelandclinic.org/health/diseases/23549-cobblestone-throat (last reviewed July 18, 2022).

Petitioner with "[a]llergic sinusitis," elevated blood pressure, and back pain. Id. He prescribed Metaxalone for Petitioner's back pain and administered Depo Medrol 40mg intramuscularly. Id. at 33.

Two days later, on August 19, 2015, Petitioner presented to Doctors Hospital of Augusta ("Doctors Hospital") Emergency Room ("ER") complaining of weakness. Pet. Ex. 4 at 1770. Associated symptoms included fatigue and falls. Id. She had not been "feeling well since taking [P]revnar vaccination at [PCP] office earlier in week." Id. Review of systems documented that Petitioner had nasal congestion and sore throat but she denied fever, chills, shortness of breath, and cough. Id. at 1770-71. Physical examination was normal. Id. at 1772. Petitioner did not have lymphadenopathy, she had normal breath sounds, and her neurological examination was normal. Id. Sodium levels were low at 129 (range 136-145) and WBC count was 11.01 (range 4.0-11.0). Id. at 1773. Computerized tomography ("CT") of the head did not show hemorrhage. Id. at 1774. ER physician Dr. John Owensby's diagnosis was weakness, and he noted that Petitioner had some hyponatremia (low sodium) "which could explain her weakness." Id. at 1775. Petitioner was discharged home. Id. at 1776.

On August 21, 2015, emergency medical services ("EMS") personnel were dispatched to Petitioner's home for a complaint of progressive weakness for 10 days. Pet. Ex. 5 at 4. Petitioner reported that she began feeling weak ten days prior and the weakness had progressively worsened. Id. She reported that she felt weak and was unable to walk. Id. She was able to stand with assistance. Id.

Petitioner was transported by ambulance to Doctors Hospital, where she was evaluated in the ER by Davis Mellick, P.A., and Dr. Robert H. Webb. Pet. Ex. 4 at 1093-99. She complained of weakness with an onset date of August 18, 2015, four to five days prior. Id. at 1093. She also reported fatigue and URI.[14] Id. She had generalized weakness of her upper and lower extremities bilaterally and reported falls. Id. She had been seen the prior Wednesday in the ER (August 19), with "extensive workup including CT with no acute findings." Id. In review of systems, she denied malaise, fever, chills, fatigue, and lethargy. Id. She also denied shortness of breath, cough, and wheezing. Id. at 1094. Physical examination revealed normal breath sounds, and neurological examination was normal. Id. at 1095. Laboratory studies showed hyponatremia. Id. at 1096. Petitioner was admitted with diagnoses of acute hyponatremia and generalized weakness. Id. at 1098.

On admission, Petitioner was seen by hospitalist Dr. Subhose Bathina, who documented a detailed history. Pet. Ex. 4 at 1107. Petitioner reported being seen in urgent care on August 14, by her PCP on August 17, and in the ER on August 19 before returning to the ER by ambulance on August 21. Id. Petitioner reported that she

[14] Although Petitioner reported that she had a URI, her medical records do not state that she had been given that diagnosis.

> initially started having mild weakness about a week prior. She was diagnosed with bronchitis[15] at urgent care and . . . put on Zithromax. . . . [S]he followed up with her [PCP] on [August 17] and . . . [she] was still having generalized weakness and mild cough and [] was seen on [August 19] in our [ER], where she [] had a CT head, [] which showed no acute hemorrhage or mass effect. The reason she had a CT head, she had an episode of fall and was complaining of mild headache on [August 19].

Id. At the ER on August 19, Petitioner also had a chest X-ray, which showed that her "[l]ungs were well expanded and clear of infiltration or consolidation." Id. On August 20, Petitioner became so weak, she had difficulty walking, requiring assistance from her husband. Id. Petitioner also reported she had not been able to eat well for the past week. Id.

Physical examination showed that Petitioner appeared "mildly dehydrated and weak." Pet. Ex. 4 at 1107. She had good range of motion of all her extremities and no focal neurological deficits. Id. at 1107, 1109. Petitioner had "decreased salivary pool." Id. at 1107-08. Lung sounds revealed "[e]qual air entry bilaterally." Id. at 1108. Petitioner was diagnosed with hyponatremia due to dehydration versus renal etiology, hypokalemia, hypertension, hyperlipidemia, mild-to-moderate dehydration, and "[g]eneralized weakness[] probably secondary to hyponatremia and dehydration." Id. at 1109. Dr. Bathina opined that Petitioner "[did] not have any source of infection and she [was] not going to be started on any IV antibiotics." Id.

After admission, on August 21, Petitioner was seen by Dr. Mark T. Smith in consultation for acute hyponatremia. Pet. Ex. 4 at 1111. Dr. Smith noted that on August 1, Petitioner received a Prevnar 13 vaccine. Id. She reported that "[a]fter that, she has not quite felt the same." Id. Physical examination did not show adenopathy or nodes in the neck or axillary region, and her chest was clear. Id. at 1112. Regarding hyponatremia, Dr. Smith suspected that she had "hypovolemic hyponatremia." Id. He planned to recheck her laboratory work, and to follow along. Id.

On August 25, 2015, Petitioner was seen in consultation by neurologist Dr. Charles R. Wolf. Pet. Ex. 4 at 1113-16. He noted that "[a]pproximately [two] weeks ago, [Petitioner] noted development of malaise, fatigue[,] and mild cough. There was also a single day of sneezing." Id. at 1113. Petitioner repeated her history, which was documented by Dr. Wolf. Id. Dr. Wolf documented Petitioner "noted perhaps slight weakness" on August 18, which worsened by the next day, and continued to progressively worsen. Id. Dr. Wolf performed a physical examination. Id. at 1115. His impression was GBS. Id. He noted

> [t]he weakness developed on approximately [August 18] and subsequently worsened. [Petitioner] has generalized extremity weakness . . . ; there is [a] slight decreased right nasolabial fold and perhaps slight decrease in forceful eye closure; [and] there have been no problems with dysphagia or dysarthria or ventilation.

[15] Petitioner reported that she had been diagnosed with bronchitis, but her medical records do not show that she was given that diagnosis at any time in August 2015.

> [Petitioner] is areflexic. Blood pressure has been somewhat elevated. [Petitioner's] hyponatremia is likely related to her [GBS]. Potential antigenic trigger to the process would be [Prevnar 13[16]] that she received on [August 1] or [URI] in early August.

Id.

Dr. Wolf ordered intravenous immunoglobulin ("IVIG") to begin the next day, August 26, and an electromyography ("EMG")/ nerve conduction study ("NCS"). Pet. Ex. 4 at 1115-16. He also ordered Petitioner be transferred to intensive care unit ("ICU") for management. Id. at 1115. On admission to the ICU, the critical care provider took a history noting that Petitioner received a Prevnar 13 vaccine on August 1, and about a week later, Petitioner "noticed she 'missed stepped' more frequently," but she did not think much about it. Id. at 1117. The critical care provider noted that the possible triggers of Petitioner's GBS were Prevnar 13 and URI. Id. at 1123. This sentence about triggers is noted throughout Petitioner's hospital records. See, e.g., id. at 1123, 1130, 1135, 1139, 1149, 1154, 1249.

On August 26, 2015, EMG/NCS showed sensorimotor demyelinating polyneuropathy consistent with GBS. Pet. Ex. 4 at 1110, 1452-54.

During her hospitalization, Petitioner developed left lower lobe atelectasis, thrush, dysphagia with high risk of aspiration, left pleural effusion, shortness of breath, leukocytosis possibly due to aspiration pneumonia, and bibasilar densities in the lungs. Pet. Ex. 4 at 1143-44, 1149-51, 1163, 1175, 1430. On August 27, she complained that she did not feel that her weakness was worsening but she did not think she was improving. Id. at 1178. She had difficulty swallowing. Id.

Petitioner completed IVIG on August 31 and was discharged on September 2, 2015. Pet. Ex. 4 at 1091-92. Her discharge diagnoses included GBS, hyponatremia, pharyngeal dysphagia, bibasilar infiltrates, and oral candidiasis. Id. at 1091. Her discharge summary noted that her GBS was "thought to be due to viral illness or recent pneumococcal vaccination." Id. at 1092. She received IVIG for five days "with some improvement in her motor weakness." Id. Petitioner was discharged to rehabilitation. Id.

On September 2, 2015, Petitioner was transferred to the hospital rehabilitation unit to "increase her functional independence," due to a number of medical concerns including weakness, impaired mobility and activities of daily living ("ADLs"), impaired gait, GBS, dysphagia, electrolyte abnormality, diarrhea, and neuropathic pain. Pet. Ex. 4 at 95. Dr. Krishan Khera's diagnosis was "[GBS] w[ith] ascending paralysis." Id. at 95-96. A rehabilitation program was established to increase Petitioner's strength, endurance, and range of motion/flexibility, coordination, and impaired balance. Id. at 106. While in rehabilitation, Petitioner developed rectal bleeding, and sigmoidoscopy noted a rectal ulcer and internal hemorrhoids. Id. at 520-21. Abdominal CT showed fatty liver and a small ventral hernia. Id. at

[16] For clarity, all references to a Pneumovax vaccine have been changed to Prevnar 13 as the parties stipulated Petitioner received a Prevnar 13 vaccine. Joint Submission at 1.

562-63. Petitioner was discharged to a rehabilitation facility on October 8, 2015. Id. at 95, 99, 601; Pet. Ex. 6 at 13.

Petitioner completed her physical and occupational therapy at Harrington Park Rehabilitation. See generally Pet. Ex. 6. No complications were reported during this extended stay, and she made steady gains in strength and independence. See generally id. In late December 2015, Petitioner was discharged to home, where her sister-in-law provided needed in-home assistance. Id. at 84, 287, 331.

At a follow-up appointment on January 5, 2016 with her PCP Dr. Price, Petitioner was noted to have increased strength in her arms and increased mobility. Pet. Ex. 2 at 28. Her legs remained extremely weak but were improving. Id. His assessment was "[GBS] following vaccination."[17] Id. at 30. He also listed GBS post-Prevnar 13 vaccine under allergies.[18] Id. at 29. At follow-up with Dr. Price in February 2016, Petitioner was wearing ankle-foot orthosis ("AFO")[19] splints and still had significant weakness of her distal legs. Id. at 25-27.

On March 3, 2016, Petitioner presented to neurologist Dr. Thomas R. Swift. Pet. Ex. 7 at 1-4. Petitioner reported developing generalized weakness and fatigue one week after receiving a Prevnar 13 vaccination on August 1, 2015. Id. at 1. She had persistent bilateral foot drop. Id. at 2. No lumbar puncture had been done, but the prior abnormal EMG/NCS results were noted. Id. Dr. Swift's examination showed normal tone of the upper extremities with 5/5 strength and increased tone of the distal lower extremities with limited dorsiflexion bilaterally (3/5). Id. at 3. Sensation was intact on the left extremities but decreased to pinprick, vibration, and light touch on the right upper and lower extremity. Id. Reflexes were 2+ throughout, except for being trace at the ankles bilaterally. Id. at 4. Heel and toe walking were intact, but gait was unsteady due to high stepping from foot drop. Id. Impression was improving GBS. Id. Petitioner was directed to continue with physical and occupational therapy and to follow-up in six months. Id.

By September 27, 2016, Petitioner reported doing much better. Pet. Ex. 2 at 13. Dr. Price noted that she was able to ambulate without a walker. Id. Her strength in her lower extremities was "greatly improved." Id. She was also able to go up steps with minimal assistance. Id. Examination showed relatively normal strength of the arms and legs. Id. at 14. Dr. Price's assessment was "[GBS] following vaccination." Id.

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[17] Dr. Price's records document "[GBS] following vaccination" or "due to vaccination" many times. Pet. Ex. 2 at 2, 4, 7-9, 11, 13-23, 25, 27-28, 30.

[18] His records continually noted this allergy. See Pet. Ex. 2 at 2, 7, 10, 14, 17, 20, 23, 26, 29.

[19] AFO refers to "any orthotic device for the lower limb that encloses the ankle and foot and does not extend above the knee; often there is a cuff or other device in the region of the knee or upper calf to take weight off the limb." Ankle-Foot Orthosis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=95032 (last visited Oct. 17, 2024).

On May 11, 2017, Petitioner was "doing very well." Pet. Ex. 2 at 6. She was walking much better and was only having to use an assistive device occasionally. Id. She had "hyperesthesia [of the] soles of [her] feet and dysesthesia of [her] left arm and left knee cap." Id. Dr. Price's records noted "[GBS] due to vaccination . . . essentially resolved; off walker and out of therapy." Id. at 8.

When Petitioner saw Dr. Price on September 21, 2017, she reported that she continued to have "some weakness of [her] left shoulder and neuropathic sensation in [her] left knee and feet related to residuals of her [GBS]." Pet. Ex. 2 at 1. She was walking at the gym three times weekly, cooking for herself, and active in her volunteer work. Id.

E. Expert Reports[20]

1. Petitioner's Expert, Dr. Salvatore Q. Napoli[21]

a. Background and Qualifications

Dr. Napoli is a board-certified neurologist licensed in Massachusetts. Pet. Ex. 8 at 3; Pet. Ex. 28 at 2. He received his M.D. from Albany Medical College followed by an internship and neurology residency at Albany Medical Center. Pet. Ex. 28 at 2. Dr. Napoli completed clinical fellowships in neurophysiology, neuroimmunology, and multiple sclerosis ("MS") in Boston, Massachusetts. Id. at 1-2. Dr. Napoli is currently the President, Owner, and Medical Director of Neurology Center of New England and MS Center of New England. Id. at 1. He is also on the medical staff at two hospitals. Id. Dr. Napoli's duties include "direct clinical care of [MS] and neuroimmunology patients." Pet. Ex. 8 at 2. He has published several articles in peer-reviewed journals, as well as abstracts, and given presentations. Pet. Ex. 28 at 6-8.

b. Opinion

i. Althen Prong One

Dr. Napoli opined that more likely than not, the Prevnar 13 vaccine can cause GBS. Tr. 12-13. He offered the theory of molecular mimicry as the mechanism involved. Tr. 45. He defined molecular mimicry as immunologic cross-reactivity between the vaccine and host peripheral myelin protein. Id. In describing the mechanism, Dr. Napoli explained that it is "like friendly fire" where the "immune system assesses this protein that's seen as foreign but in reality there's homology with your own body." Tr. 47.

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[20] Although the undersigned has reviewed all the expert reports, for the sake of brevity, this Ruling does not include every detail of the experts' opinions. Instead, the undersigned focuses on the experts' material opinions, as they relate to the relevant issue of causation.

[21] Dr. Napoli provided three expert reports and testified at the hearing. Pet. Exs. 8, 20, 29; Tr. 3. The undersigned provides only a brief summary of Dr. Napoli's opinions, since the more substantive causal theories are set forth in the expert reports by Dr. Steinman.

In support of the theory of molecular mimicry generally as a reliable theory of causation, Dr. Napoli cited a paper by Lahesmaa et al.,[22] about molecular mimicry and its role in causing arthropathies. Tr. 47-48 (citing Pet. Ex. 12). Moving to vaccinations, Dr. Napoli referenced Schonberger et al.,[23] an article describing GBS cases following the National Flu Immunization Program for A/New Jersey flu vaccine in the 1970s. Tr. 48-49 (citing Pet. Ex. 13). Schonberger et al. determined there was an increase in reports of GBS after the vaccination campaign. Pet. Ex. 13 at 2.

Dr. Napoli also cited a paper by Haber et al.,[24] published in 2009, which reviewed articles published from 1950 to 2008, to ascertain "the current body of evidence" about vaccine-associated GBS. Tr. 51-52; Pet. Ex. 15 at 2-3. The authors noted that GBS was an immune-mediated illness "resulting from the generation of autoimmune antibodies that cross-react with epitopes on peripheral nerves, leading to nerve damage." Pet. Ex. 15 at 3. Thus, Haber et al. acknowledged the mechanism of molecular mimicry, as described by Dr. Napoli. See id. Haber et al. also noted that "[v]arious vaccines have also been temporally associated with GBS." Id. at 4. GBS was noted to be associated with the 1976-1977 flu vaccine, two types of rabies vaccinations, and the oral polio vaccine. Id. at 6-7. The review did not include a reference to the pneumococcal conjugate vaccine given here.[25] See id. at 2-13. Dr. Napoli cited it for support of his posited theory of molecular mimicry. See Tr. 51-52.

In further support of his opinions, Dr. Napoli cited case reports of GBS after pneumococcal vaccinations. The first was a case report by Ravishankar.[26] Pet. Ex. 16. Quoting Ravishankar,

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[22] R. Lahesmaa et al., Molecular Mimicry Between HLA B27 and *Yersinia*, *Salmonella*, *Shigella* and *Klebsiella* Within the Same Region of HLA α_1-helix, 86 Clinical & Experimental Immunology 399 (1991).

[23] Lawrence B. Schonberger et al., Guillain-Barre Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977, 110 Am. J. Epidemiology 105 (1979). This is also cited as Resp. Ex. E, Tab 2.

[24] Penina Haber et al., Vaccines and Guillain-Barré Syndrome, 32 Drug Safety 209 (2009). This was also cited as Resp. Ex. N, Tab 7.

[25] Prevnar 13 was approved for use in adults 50 years of age and older in December 2011, following this article's publication. See Pet. Ex. 17 at 2 (Hung Fu Tseng et al., Pneumococcal Conjugate Vaccine Safety in Elderly Adults, 5 Open Forum Infectious Diseases 1 (2018) (also cited as Resp. Ex. E, Tab 5 and Resp. Ex. N, Tab 8)).

[26] Nidhi Ravishankar, Guillain-Barre Syndrome Following PCV Vaccine, 2 Clinics Surgery 1413 (2017).

> [a] 66-year old female with a past medical history of hypertension, hyperlipidemia, gastroesophageal reflux disease presented to her local clinic [i]n January 2015 for an annual exam[ination]. She was on the cusp of retirement and was told by her physician to receive all the immunizations. She received the first dose of [Prevnar 13] in January 2015 and then the second dose of [pneumococcal polysaccharide vaccine ("PPSV23")[27]] in August 2015. . . . In September 2015, the patient began to feel weakness in the knees but dismissed it thinking it was mild arthritis. Few days later (approximately 41 days), she was unable to move her legs at all.

Id. at 1.

The next paper referenced by Dr. Napoli was by Tseng et al., a Kaiser Permanente retrospective study comparing the safety of the Prevnar 13 vaccine with PPSV23. Pet. Ex. 17 at 2. There were four cases of GBS after vaccination with Prevnar 13 and eight after PPSV23. Id. at 7 tbl.3. From a clinical trial, a 78-year-old woman developed GBS after receiving the Prevnar 13 vaccine that was considered "possibly related" to vaccination. Id. at 3. And there were three cases of GBS noted in the Vaccine Adverse Event Reporting System ("VAERS") database. Id.

In addition to the study by Tseng et al., Dr. Napoli cited to the El Khatib et al.[28] report of GBS following infection with *Streptococcus pneumoniae* ("*S. pneumoniae*"), the infection which Prevnar 13 protects against. Tr. 113 (citing Pet. Ex. 14). El Khatib et al. reported on a 13-year-old who complained of progressive lower extremity weakness and episodes of choking. Pet. Ex. 14 at 2. Subsequently he developed respiratory distress and septic shock, and blood cultures revealed *S. pneumoniae.* Id. at 2-3. The "history of inability to bear weight[] that was followed by choking with his clinical deterioration suggested [] the diagnosis of [GBS] in particular especially because of absent deep tendon reflexes." Id. at 3. GBS could not be confirmed by lumber puncture due to his unstable status. Id. The authors suggested the possibility of an antigen triggered immune response due to molecular mimicry. Id.

Lastly, Dr. Napoli testified that he has diagnosed vaccine-related GBS in approximately six patients, although he did not recall whether any of the patients had received the Prevnar 13 vaccination prior to their GBS. Tr. 78-79.

At the hearing on cross-examination, Dr. Napoli explained that vaccine injuries cannot be proven epidemiologically, and that such studies have not shown a causal association between Prevnar 13 and GBS. Tr. 117-19. He also agreed that he has not identified any specific homology between the Prevnar 13 vaccine and a host target or myelin basic protein. Tr. 119. But he stated that as a clinician he would not need proof of homology to assess causation, although he believed there is homology. Tr. 120. Further, post-vaccination GBS is too rare to be

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[27] See Pet. Ex. 50 (package insert).

[28] Hassan El Khatib et al., Case Report: Guillain-Barre Syndrome with Pneumococcus – A New Association in Pediatrics, 11 IDCases 36 (2018).

captured by epidemiological studies. Tr. 149. He also agreed that case reports do not prove causal associations. Tr. 153-54.

ii. Althen Prongs Two and Three

Dr. Napoli opined that there was a logical sequence of cause and effect between the vaccination and Petitioner's GBS, and that her GBS was not caused by infection. Tr. 15-16, 59-60. He based his opinions on the clinical course, and the fact that Petitioner had a "fulminant" case. Id. Dr. Napoli testified "the key" is that based on Petitioner's medical records, "I almost would think 100 percent of doctors would not give this vaccine again to this patient." Tr. 61.

Further, Petitioner's treating physicians' Dr. Price and Dr. Wolf believed that her GBS was "consistent with a vaccine-induced injury, related to the vaccine and also noted it as an allergy." Tr. 61. For example, Dr. Price's records note Petitioner had GBS due to vaccination and also state that Petitioner has an allergy to the vaccination. Tr. 64-65 (citing Pet. Ex. 2 at 2).

Moreover, Dr. Napoli opined that Petitioner did not have an alternate cause for her GBS. Tr. 15-16. He opined that infection was not the etiology. Tr. 16, 68, 75. He gave several reasons for his opinion. See Tr. 66-68, 75-76. First, she had a history of recurrent allergic sinusitis, and second, there was no history of infection prior to the onset of her GBS. Tr. 75-76. Third, Petitioner's treating physicians did not attribute her GBS to infection. Tr. 66-68.

Dr. Napoli opined that Petitioner had allergic sinusitis, not sinusitis due to infectious causes, prior to vaccination. Tr. 70. The fact that she was prescribed a Z-Pak was "to be on the safe side" and to "make sure it [didn't] develop into something bacterial." Id.

Dr. Napoli reviewed pertinent portions of Petitioner's medical records showing that Dr. Wolf considered both the vaccination and an URI as potential triggers of her GBS. Tr. 129-30 (citing Pet. Ex. 4 at 1115). However, when Petitioner was seen and treated by Dr. Wolf, it was Dr. Napoli's opinion that she did not have any signs of infection. Tr. 134.

Regarding the temporal association between vaccination and onset of GBS, Dr. Napoli opined Petitioner's onset occurred at approximately two to three weeks post-vaccination, well within the time frame reported in the literature for GBS to occur post-vaccination. Tr. 57. Petitioner's onset manifested as back pain, malaise, fatigue, weakness, and gait problems. Id. Langmuir et al.,[29] reported peak incidence of GBS two to three weeks following vaccination, and an outside range of eight weeks. Pet. Ex. 18 at 15, 16 tbl.7, 16 fig.1.

[29] Alexander D. Langmuir et al., An Epidemiologic and Clinical Evaluation of Guillain-Barré Syndrome Reported in Association with the Administration of Swine Influenza Vaccines, 119 Am. J. Epidemiology 841 (1984).

2. Petitioner's Expert, Dr. Lawrence Steinman[30]

a. Background and Qualifications

Dr. Steinman is board certified in neurology and has practiced neurology at Stanford University for over 43 years. Pet. Ex. 32 at 2; Pet. Ex. 33 at 1-2. He received his B.A. from Dartmouth College in 1968 and his M.D. from Harvard University in 1973. Pet. Ex. 33 at 1. Thereafter, he completed a surgery internship, pediatrics residency, and pediatric and adult neurology residency at Stanford University Hospital, as well as three fellowships, including one in clinical immunology. Id. Dr. Steinman is currently a Professor at Stanford University. Id. Dr. Steinman "is actively involved in patient care" and "ha[s] cared for hundreds of adults and children with various forms of inflammatory neuropathy, [GBS], transverse myelitis, acute disseminated encephalomyelitis[], neuromyelitis optica[,] and [MS]." Pet. Ex. 32 at 2. He has authored or co-authored over 600 publications. Pet. Ex. 33 at 5-50. Dr. Steinman has authored papers on molecular mimicry, as demonstrated by his CV. See id. One of Dr. Steinman's specialties is in the area of MS, and he has received a Charcot Prize for Lifetime Achievement due to his research in MS. Pet. Ex. 32 at 3. In 2015, he was elected to the National Academy of Sciences. Id. Dr. Steinman is also a member in the National Academy of Medicine. Id.

b. Opinion

i. Althen Prong One

Dr. Steinman opined that the Prevnar 13 vaccination can cause GBS. Pet. Ex. 32 at 1-2, 27. Dr. Steinman's expert reports and opinions focused on how the Prevnar 13 vaccine can trigger GBS via molecular mimicry.[31] Pet. Ex. 32 at 1-2, 6. Dr. Steinman agreed with Respondent's expert, Dr. Whitton, that molecular mimicry only rarely causes disease. Pet. Ex. 62 at 2.

Dr. Steinman reviewed the components of the vaccine and the main targets of the human immune response in GBS and proposed two mechanisms whereby molecular mimicry can trigger GBS following Prevnar 13 vaccination. The first involves homology between the components in the vaccine and phosphoglycerol components in the myelin and axons of peripheral nerves. Pet. Ex. 32 at 6-15. The second involves homology between CRM_{197} in the vaccine and Contactin-1, a protein found in humans. Id. at 15-26.

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[30] Dr. Steinman provided two expert reports. Pet. Exs. 32, 62. He did not testify at the hearing, as his reports were submitted after the entitlement hearing.

[31] Dr. Steinman examined the immune response to phosphoglycerol in the myelin lipids in the context of GBS, specifically phosphatidyl-ethanolamine, phophatidyl-choline, and phosphatidylserine, based on Ho et al. See Pet. Ex. 32 at 7 (citing Pet. Ex. 39 (Peggy P. Ho et al., Identification of Naturally Occurring Fatty Acids of the Myelin Sheath That Resolve Neuroinflammation, 4 Sci. Translational Med. 1 (2012))).

1. Phosphoglycerol[32] in Serotypes 18C and 23F

The first mechanism described by Dr. Steinman involves homology between phosphoglycerol in the Prevnar 13 vaccine, present in the antigens of *S. pneumoniae* serotypes 18C and 23F, and phospholipids, specifically glycerophosphate and glycerocholine in the human myelin sheath. Pet. Ex. 32 at 6-15; see also Pet. Ex. 42 at 24 (Prevnar 13 package insert).

Based upon information obtained from the vaccine patent,[33] Dr. Steinman explained that the glycerol phosphate side chains in the vaccine are necessary for its immunogenicity.[34] Pet. Ex. 32 at 8. Dr. Steinman cited an article by Chang et al.[35] to support his opinion that the phosphoglycerol component is preserved during the process of making the vaccine. Pet. Ex. 32 at 8-10 (citing Pet. Ex. 45 at 1). Chang et al. showed "that glycerol-phosphate must be preserved for conserving adequate antigenicity of the 18C capsular polysaccharide." Pet. Ex. 45 at 1.

Dr. Steinman explained how the data from the vaccine patent and the studies relate to the pathogenesis of GBS. Pet. Ex. 32 at 6-10. He opined that phospholipids[36] are the targets of antibodies in GBS. Id. at 7. He asserted that antibodies to phosphoglycerol structures interact with myelin components triggering GBS. Id. Based on his own research, Dr. Steinman explained that "phospholipids are components of the myelin sheath in humans, and they are targeted by antibodies" leading to neuroinflammation in GBS. Id.

In support of this aspect of his opinion, Dr. Steinman relied on several articles. The first was authored by Ho et al. and Dr. Steinman is also a named author. Pet. Ex. 39. The authors showed that in the demyelinating disease MS, autoantibodies primarily target a phosphoglycerol

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[32] Phospho- is a "prefix [] indicating the presence of phosphorus in a compound." Stedman's Medical Dictionary 1486 (28th ed. 2006). Glycerol is "[a] sweet viscous fluid obtained by the saponification of fats and fixed oils; used as a solvent, as a skin emollient, . . . and as a vehicle and sweetening agent." Stedman's at 820.

[33] The patent is filed as Petitioner's Exhibit 47. The description of the glycerol phosphate side chain in 18C can be found at page 34, and a diagram of the chemical structure is on page 6.

[34] Immunogenicity is defined as "the property that endows a substance with the capacity to provoke an immune response, or the degree to which a substance possesses this property." Immunogenicity, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=24893 (last visited Oct. 17, 2024).

[35] Janoi Chang et al., Relevance of O-acetyl and Phosphoglycerol Groups for the Antigenicity of the *Streptococcus pneumoniae* Serotype 18C Capsular Polysaccharide, 30 Vaccine 7090 (2012).

[36] Phospholipid is defined as "any lipid that contains phosphorus, including those with a glycerol backbone (phosphoglycerides and plasmalogens) . . . . Phospholipids are the major form of lipid in all cell membranes." Phospholipid, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=38759 (last visited Oct. 17, 2024).

component of myelin. Pet. Ex. 32 at 7 (citing Pet. Ex. 39 at 1). The "findings indicate[d] that myelin phospholipids are targeted by autoimmune responses in MS." Pet. Ex. 39 at 9. Moreover, "[l]ipids constitute 70% of the myelin sheath." Id. at 1; see also Pet. Ex. 62 at 4-5 (explaining that Barbar et al. "concluded that binding to the phospho-containing group in phenylphsosphocholine was retained, no matter what the structure was that was attached to it") (citing Pet. Ex. 63).[37]

In Gilburd et al.,[38] the authors "studied the reactivity of GBS sera with various phospholipids which are known to be important constituents of myelin, and serve as autoantigens in other autoimmune conditions." Pet. Ex. 43 at 2. Six of the 16 patients with GBS had autoantibodies to various phospholipids. Id. at 2, 5. However, the authors suggested this was "probably [] a result of [] myelin damage rather than [the] cause of demyelination." Id. at 2, 6.

Nakos et al.[39] studied anti-phospholipid antibodies in nine patients with GBS. Pet. Ex. 44 at 1. All nine patients in the study had anti-phospholipid antibodies and no such antibodies were detected in the nine control subjects. Id. The authors "detected a wide range of anti-phospholipid antibodies in patients with idiopathic GBS," and "[a]ll nine GBS patients developed anti-phospholipid antibodies directed against at least one lipid during the course of the disease." Id. at 5. They wrote, "[t]he association of GBS and certain autoimmune diseases, including systemic lupus erythematosus, is well recognized," and they noted "[h]igh levels of anti-phospholipid antibodies were expressed in a patient with lupus like syndrome who developed secondary GBS." Id. at 6. The authors explained that "[i]t is thought that whenever polyneuropathy occurs in the context of autoimmune diseases, mainly in systemic lupus erythematosus, where anti-phospholipid activity already exists, these antibodies can cross-react with phospholipids and mediate damage in neural structures containing the particular phospholipids." Id. Of note, the GBS patients in the Nakos et al. study had primary GBS (relevant here), not the secondary form like that which occurs in patients with lupus. Id. The authors also observed anti-ganglioside antibodies, but only in 44% of the patients. Id. They concluded,

> [i]t is not well understood whether these anti-phospholipid antibodies play a role in the pathogenesis of the polyneuropathy or represent a part of a more extensive immunoreaction that takes place in [] GBS. However, immunopathology in autopsies suggests that antibody mediated injury is a predominant disorder in the demyelinating form of GBS. The immune attack is

[37] Elisar Barbar et al., Binding of Phenylophosphocholine—Carrier Conjugates to the Combining Site of Antibodies Maintains a Conformation of the Hapten, 35 Biochemistry 2958 (1996).

[38] B. Gilburd et al., Autoantibodies to Phospholipids and Brain Extract in Patients with the Guillain-Barré Syndrome: Cross-Reactive or Pathogenic?, 16 Autoimmunity 57 (1993).

[39] G. Nakos et al., Anti-Phospholipid Antibodies in Serum from Patients with Guillain-Barré Syndrome, 31 Intensive Care Med. 1401 (2005).

> directed against components of Schwann cell[40] membrane and is accompanied by the characteristic feature of vesicular demyelination. Therefore, it is crucial to investigate how anti-phospholipid antibodies are related to specific antigens in Schwann cell membrane.
>
> . . . .
>
> Our findings suggest that in GBS there is a more extensive immune reaction, beyond the well known antiganglioside production, which has been related to the demyelination of the peripheral nerves.

Id. at 6-7.

Matà et al.[41] was referenced by Dr. Steinman to further support his opinions. Pet. Ex. 62 at 18 (citing Pet. Ex. 73). In that study, anti-cardiolipin antibodies were increased in some GBS patients as compared to controls. Pet. Ex. 73 at 4. The authors observed that the pathogenesis of GBS is complex, and while autoantibodies to gangliosides constitute the predominant autoantibody response in patients, "antibodies to other lipid antigens can be detected in GBS in a lower but statistically significant proportion of cases." Id. at 5. They found "increased autoantibody titers to cardiolipin [] in 20% of GBS patients." Id.

In his supplemental expert report, Dr. Steinman also cited to Terryberry et al.,[42] for the purpose of reiterating one of his principle points, which is that gangliosides are not the only target applicable to molecular mimicry in GBS and that antibodies to phospholipids have also been identified. Pet. Ex. 62 at 18-19 (citing Pet. Ex. 70). Terryberry et al. reported that there are "[w]ide discrepancies and variations . . . in both the type and binding characteristics of the autoantibodies associated with GBS." Pet. Ex.

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[40] Schwann cells are "any of the large nucleated cells whose cell membrane spirally enwraps the axons of myelinated peripheral neurons and is the source of myelin; a single Schwann cell supplies the myelin sheath between two nodes of Ranvier." Schwann Cell, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=64407 (last visited Oct. 17, 2024). The nodes of Ranvier are "constrictions occurring on myelinated nerve fibers at regular intervals of about [one] mm; at these sites the myelin sheath is absent and the axon is enclosed only by Schwann cell processes." Nodes of Ranvier, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=93095 (last visited Oct. 17, 2024).

[41] Sabrina Matà et al., Anti-GM1, Anti-Central Myelin Proteins, and Anti-Cardiolipin Autoantibodies During Plasma-Exchange in Guillain-Barré Syndrome (GBS), 13 J. Clinical Apheresis 155 (1998).

[42] Jeff Terryberry et al., Myelin- and Microbe-Specific Antibodies in Guillain-Barré Syndrome, 9 J. Clinical Lab'y Analysis 308 (1995).

70 at 4. In the 56 patients with GBS, "[a]utoantibodies to phospholipids such as cardiolipin and phosphatidylcholine," along with others, are also described. Id. The authors concluded that "[c]urrent evidence supports the notion that there is no single GBS antigen. Likewise, there are multiple antecedent factors (i.e., infectious agents) for the disease, and the different myelin antigens might be related in terms of sequential and conformational homology to the various pathogens (molecular mimicry)." Id. at 5.

Lastly, Dr. Steinman cited a study by Bryson et al.[43] of antibodies directed to serotype 23F "from humans who were immunized with a pneumococcal vaccine ([PPSV23]) that contained 23F.[44] Pet. Ex. 32 at 10-13 (citing Pet. Ex. 48 at 2). He explained Bryson et al. showed X-rays of "human antibody targeting the 23F component of *S. pneumonia[e]*." Pet. Ex. 32 at 11 (citing Pet. Ex. 48 at 2). Dr. Steinman opined the X-rays demonstrate the "human antibody response to 23F after the human received a pneumococcal vaccine intended to elicit antibodies to 23F." Id. at 12. Dr. Steinman concluded that the "data from the Bryson [et al.] article demonstrate unequivocally that the immune response to the serotype 23F component of [PPSV23] targets the phosphoglycerol in serotype 23F." Id. at 14 (emphasis omitted).

In his second expert report, Respondent's expert, Dr. Whitton discussed Bryson et al. and opined that the "Bryson antibodies recognize[d] predominantly polysaccharides," not phosphoglycerol. Resp. Ex. P at 8. Dr. Steinman agreed, stating that "is my whole point." Pet. Ex. 62 at 7. Dr. Steinman explained that "[t]he antibodies recognize phosphoglcerol and the 23F polysaccharide." Id. Using a metaphor, he compared the antibodies affinity to the phosphate group to the "hook on an aircraft carrier." Id. at 8. Dr. Steinman explained that he and Dr. Whitton disagree about whether the antibodies bind to phosphoglycerol but maintained, based on Ho et al.[45] and Barbar et al.,[46] that "this binding to the phosphate group is well described in the literature, that it is common and . . . often critical." Id. at 9 (citing Pet. Exs. 39, 63).

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[43] Steve Bryson et al., Structures of Preferred Human IgV Genes–Based Protective Antibodies Identify How Conserved Residues Contact Diverse Antigens and Assign Source of Specificity to CDR3 Loop Variation, 196 J. Immunology 4723 (2016).

[44] Serotype 23F is included in both Prevnar 13 and PPSV23. See Pet. Ex. 42 (Prevnar 13 package insert); Pet. Ex. 50 (PPSV23 package insert).

[45] Ho et al. examined the role of lipids in autoimmune demyelination, specifically "whether lipids in the myelin sheath are targeted by autoimmune responses in MS." Pet. Ex. 29 at 1, 9. They found "myelin phospholipids are targeted by autoimmune responses in MS and that these myelin phospholipids represent a natural anti-inflammatory class of compounds that have potential as therapeutics for MS." Id. at 9.

[46] Barbar et al. was referenced in Dr. Steinman's second report. See Pet. Ex. 62 at 4-5, 7-10, 13-14. The goal of the study was to "characterize carrier contributions to hapten-antibody interactions." Pet. Ex. 63 at 9. They found that "the conformation of the bound hapten is unaffected by the associated carrier residues." Id. at 2. Dr. Steinman cited the paper for the proposition that the "phospho-containing group . . . was retained, no matter what the structure was that was attached to it." Pet. Ex. 62 at 4.

In summary, Dr. Steinman's first theory is based on molecular mimicry, and he opined antibodies to the phosphoglycerol structures in Prevnar 13 (via serotypes 18C and 23F) target an immune response in phospholipids in the myelin of peripheral nerves, triggering GBS. Pet. Ex. 32 at 6-15.

2. CRM_{197} and Contactin-1

The second homology posited by Dr. Steinman is between the protein carrier in the vaccine, CRM_{197},[47] and Contactin-1,[48] targeted in some cases of GBS. Pet. Ex. 32 at 15. Prevnar 13 is a conjugate vaccine in which the individual polysaccharides of the capsular antigens of *S. pneumoniae* are linked to a non-toxic diphtheria CRM_{197} protein. Id. at 6 (citing Pet. Ex. 42 at 24). "CRM_{197} is a nontoxic variant of diphtheria toxin," used as a protein carrier which makes the vaccine more immunogenic. Id. at 6, 15 (quoting Pet. Ex. 42 at 24). CRM_{197} differs from diphtheria toxin by only one amino acid, and is therefore not toxic. Id. at 6, 24; see also Pet. Ex. 60 at 1.[49]

Again, based on his own research, Dr. Steinman determined that molecular mimicry might occur between CRM_{197} and Contactin-1, a molecule that has been identified in patients with GBS. Pet. Ex. 32 at 15. Dr. Steinman relied on Miura et al., a study done on patients with CIDP. Id. (citing Pet. Ex. 52). Miura et al. focused their research on patients with CIDP, but used sera from patients with GBS, MS, and healthy patients as controls. Pet. Ex. 52 at 2. They found that five of the 200 patients with GBS had anti-Contactin-1 immunoglobulin G ("IgG") antibodies. Id. at 3, 6 tbl.2.

The Miura et al. authors explained the theory of pathogenesis relevant to Dr. Steinman's theory, as it relates to Contactin-1. They stated,

> [c]ell adhesion molecules play a crucial role in the formation of the nodes of Ranvier and in the rapid propagation of the nerve impulses along myelinated axons. In the peripheral nerves, the domain organization of myelinated axons

[47] Protein carrier "CRM_{197} is a nontoxic variant of diphtheria toxin isolated from cultures of *Corynebacterium diphtheriae* strain C7 (β197) grown in a casamino acids and yeast extract-based medium." Pet. Ex. 42 at 24 (Prevnar 13 package insert).

[48] Contactin-1, or CNTN1, "is a key axonal adhesion molecule, which interacts with CNTNAP1 (previously known as Caspr1) on the axon and neurofascin-155 on the glial side, and is essential for the formation of the paranodal septate-like junction." Pet. Ex. 52 at 2 (Yumako Miura et al., Contactin I IgG4 Associates to Chronic Inflammatory Demyelinating Polyneuropathy with Sensory Ataxia, 138 Brain 1484 (2015)).

[49] Michael Bröker et al., Biochemical and Biological Characteristics of Cross-Reacting Material 197 (CRM_{197}), a Non-Toxic Mutant of Diphtheria Toxin: Use as a Conjugation Protein in Vaccines and Other Potential Clinical Applications, 39 Biologicals 195 (2011).

> depends on specific axo-glial contacts between the axonal membrane and Schwann cells at nodes, paranodes[,] and juxtaparanodes.

Pet. Ex. 52 at 2.

Miura et al. identified Contactin-1 (CNTN1) as one of the targets of autoantibodies in some patients with GBS. Pet. Ex. 52 at 3. Dr. Steinman also cited Lanz et al.,[50] an article he is a named author of, noting that antibodies to paranodal proteins are found in GBS. Pet. Ex. 56 at 3 ("Antibodies to paranodal proteins are found in MS and in both [GBS] and chronic inflammatory polyneuropathy.")).

Based on this information about the potential importance of Contactin-1, Dr. Steinman conducted a BLAST[51] search to determine whether there was homology between CRM_{197} in the vaccine and Contactin-1.[52] Pet. Ex. 32 at 15. He found a sequence[53] ("WEQ sequence") that "might be capable of inducing a neuroinflammatory disease." Id. at 23. He found it is an epitope in diphtheria toxin, which provides the basis for CRM_{197}. Id. at 23-24.

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[50] Tobias V. Lanz et al., Roadmap for Understanding Mechanisms on How Epstein-Barr Virus Triggers Multiple Sclerosis and for Translating These Discoveries in Clinical Trials, 12 Clinical & Translational Immunology e1438 (2023).

[51] A BLAST (Basic Local Alignment Search Tool) search "finds regions of similarity between biological sequences. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance." BLAST, https://blast.ncbi.nlm.nih.gov/Blast.cgi (last visited Oct. 17, 2024).

[52] For a complete explanation of Dr. Steinman's investigation, including his discussion on the number of amino acids required for homology relevant to molecular mimicry as well as the procedure he followed in conducting his BLAST searches and his research using the Immune Epitope Database ("IEDB"), see Pet. Ex. 32 at 15-25. Based on his IEDB search, Dr. Steinman was referred to a paper by Raju et al. that reported a human immune response to the diphtheria toxin and identified the WEQAKALSVE sequence. Pet. Ex. 32 at 25-26 (citing Pet. Ex. 31 at 2 (Raghavanpillai Raju et al., Epitopes for Human CD4+ Cells on Diphtheria Toxin: Structural Features of Sequence Segments Forming Epitopes Recognized by Most Subjects, 25 Euro. J. Immunology 3207 (1995))).

[53] The sequence is "WEQAKALSVE," which "has five of ten identical amino acids." Pet. Ex. 32 at 23.

Dr. Steinman responded to criticism offered by Dr. Whitton about his BLAST search. Dr. Whitton criticized the expected value ("E-value")[54] of Dr. Steinman's BLAST search, which was 2.7. Pet. Ex. 62 at 27-28, 32, 35-37. To respond, Dr. Steinman referenced the landmark study from Fujinami and Oldstone[55] showing that a short sequence of similar amino acids could induce experimental allergic encephalomyelitis ("EAE") through the mechanism of molecular mimicry. Id. at 32-37 (citing Pet. Ex. 71 at 1-3). Dr. Steinman repeated the search done by Fujinami and Oldstone, and found that their E-value was 3.8, higher than his search value of 2.7. Id. Dr. Steinman reiterated that the studies, including those authored by Gautam et al.,[56] have shown that sequences of five or six out of 11 or 12 amino acid sequences could cause paralysis in animal studies. Id. at 29 (citing Pet. Exs. 54-55, 61).

[54] Expected value, or E-value, "in statistics, [is] the value of an estimate that is the mean of its sampling distribution." Expected Value, Dorland Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=116686 (last visited Oct. 17, 2024). Relying on Silvanovich et al., Dr. Whitton opined that in a BLAST search, "the identified homology must have an E-value below a threshold of 3.9×10^{-7}. A homology with E-value larger than that threshold should be discarded." Resp. Ex. N at 42-46 (citing Resp. Ex. N, Tab Tab 29 (Andre Silvanovich et al., The Value of Short Amino Acid Sequence Matches for Prediction of Protein Allergenicity, 90 Toxicological Scis. 252 (2006)); Resp. Ex. N, Tab 31 (Andre Silvanovich et al., The use of E-scores to Determine the Quality of Protein Alignments, 54 Regul. Toxicology & Pharmacology S26 (2009))). The other Silvanovich et al. criteria provide that a sequence be at least 80 amino acids long and at least 28 of the amino acids be aligned. Id. at 42-44. Dr. Steinman opined that the Silvanovich et al. criteria are not applicable due to the findings of Fujinami and Oldstone, showing that short sequences of amino acids can induce disease. Pet. Ex. 62 at 27-32 (citing Pet. Ex. 71 (Robert S. Fujinami & Michael B. A. Oldstone, Amino Acid Homology Between the Encephalitogenic Site of Myelin Basic Protein and Virus: Mechanism for Autoimmunity, 230 Science 1043 (1985))).

[55] Fujinami and Oldstone, immunologists at Scripps, used computer analysis to identify "six consecutive amino acids" in myelin basic protein which was "sufficient to produce immunologic crossreactivity" via molecular mimicry which was shown to cause histology results similar to experimental allergic encephalomyelitis ("EAE"). Pet. Ex. 71 at 1-3.

[56] Anand M. Gautam et al., A Polyalanine Peptide with Only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis, 176 J. Experimental Med. 605 (1992); Anand M. Gautam et al., Minimum Structural Requirements for Peptide Presentation by Major Histocompatibility Complex Class II Molecules: Implications in Induction of Autoimmunity, 91 Immunology 767 (1994); Anand M. Gautam et al., A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis, 161 J. Immunology 60 (1998). Dr. Steinman is a named author in all of these papers.

In addition to the WEQ sequence, Dr. Steinman identified another sequence[57] that "has known cross-reactivity with epitopes described in humans" on the *Corynebacterium diphtheriae* microbe. Pet. Ex. 32 at 24.

Dr. Steinman opined the two sequences he found were significant due to five identical amino acids in a nervous system protein. Pet. Ex. 32 at 23. He cited a number of papers, including some that he authored or co-authored, to support his opinion that homology of just five amino acids can induce an immune response consistent with his theory here. Id. at 15-17. For example, in his 1993 paper,[58] Dr. Steinman wrote that "[a]n autoimmune response can begin even if the molecular mimicry is not quite exact." Pet. Ex. 41 at 4. He cited the Gautam et al. studies for the proposition that autoimmune encephalomyelitis could be induced with only five amino acids identical to myelin basic protein, out of short sequences of 10 amino acids. Pet. Ex. 32 at 15 (citing Pet. Exs. 54-55, 61).

In summary, Dr. Steinman averred that "th[is] theory provides actual detailed data for molecular mimics in the $CRM_{[197]}$ in the Prevnar 13 vaccine" and "shows how these mimics could trigger inflammatory neuropathy culminating in GBS." Pet. Ex. 32 at 25-26 (emphasis omitted).

3. Medical Literature

In addition to setting forth his theories, Dr. Steinman offered medical literature in support of his opinions.

He cited the same case report by Ravishankar referenced by Dr. Napoli about GBS after pneumococcal vaccination. Pet. Ex. 32 at 26 (citing Pet. Ex. 16). He also cited Haber et al.[59] Id. (citing Resp. Ex. E, Tab 4). There were 11 reports of GBS after the Prevnar 13 vaccination, one in patients aged 19 to 64, and 10 in the age range of 65 and older. Resp. Ex. E, Tab 4 at 5-6, 4 tbl.2a, 5 tbl.2b. Median onset was nine days post-vaccination and median patient age was 68 years. Id. at 5. Dr. Steinman stated that the paper "reinforces the likelihood that molecular mimicry following Prevnar 13 vaccination can cause GBS." Pet. Ex. 32 at 26 (citing Resp. Ex. E, Tab 4).

Dr. Steinman concluded that "GBS is a relatively rare illness. Numerous vaccines including Prevnar 13 can in rare instances through the theory of molecular mimicry cause GBS." Pet. Ex. 32 at 26.

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[57] The second sequence is "EYMAQACAGNRVRR." Pet. Ex. 32 at 24.

[58] Lawrence Steinman, Autoimmune Disease, 269 Sci. Am. 106 (1993).

[59] Penina Haber et al., Post-Licensure Surveillance of 13-Valent Pneumococcal Conjugate Vaccine (PCV13) in Adults Aged ≥19 Years Old in the United States, Vaccine Adverse Event Reporting System (VAERS), June 1, 2012–December 31, 2015, 34 Vaccine 6330 (2016). Petitioner did not provide the Haber et al. article cited by Dr. Steinman.

In his second report, Dr. Steinman responded to Dr. Whitton's criticism of his theories.[60] See generally Pet. Ex. 62. For example, Dr. Whitton observed *S. pneumoniae* is not known to increase the risk of GBS, and therefore he questioned "why [] the same polysaccharides in the vaccine [should] be thought" to cause GBS. Resp. Ex. P at 4. In response, Dr. Steinman explained that the Prevnar vaccine is "considerably different" than *S. pneumoniae* bacteria because its sugars are not conjugated to the protein carrier CRM_{197}, which is similar to the diphtheria toxoid. Pet. Ex. 62 at 3, 15. Dr. Steinman also noted that the vaccine, which contains an adjuvant,[61] is injected, whereas the *S. pneumoniae* bacteria enters the body through the respiratory tract. Id. at 3.

ii. Althen Prong Two

Dr. Steinman opined there was "[a] logical sequence of cause and effect showing [] the vaccination was the reason for the injury" since Prevnar 13 "has constituents that induce antibodies known to cross-react with myelin and that are found in patients with GBS." Pet. Ex. 32 at 27.

iii. Althen Prong Three

Dr. Steinman opined that Petitioner's onset of GBS was approximately three weeks after vaccination. Pet. Ex. 32 at 26. He opined this timing was "certainly consistent with the timing known for GBS and the 1976 swine [flu] immunization, often used as a surrogate in such cases" regarding timing. Id. (citing Pet. Ex. 13). Dr. Steinman concluded that the temporal relationship criteria of Althen prong three was fulfilled based on this interval. Id. at 26-27.

3. Respondent's Expert, Dr. Robert T. Naismith[62]

a. Background and Qualifications

Dr. Naismith is a board-certified neurologist licensed to practice in Missouri and Illinois. Resp. Ex. L at 3. He obtained his M.D. from Case Western Reserve University after which he completed an internal medicine internship at Barnes-Jewish Hospital and a neurology residency and MS fellowship at Washington University in St. Louis, Missouri. Id. at 1. Thereafter, he began working at Washington University School of Medicine where he is currently the

[60] The undersigned does not address most of these criticisms for the sake of brevity and relevance, though they have been carefully considered.

[61] Dr. Steinman noted that the vaccine, unlike the bacteria, contains an adjuvant (alum) but he did not opine that the adjuvant plays a role in vaccine causation. See Pet. Ex. 62 at 3. Thus, the undersigned does not find that Dr. Steinman is invoking the autoimmune/inflammatory syndrome induced by adjuvant ("ASIA") theory, as referenced by Dr. Whitton. See Resp. Ex. P at 4.

[62] Dr. Naismith testified at the hearing and provided three expert reports. Tr. 3; Resp. Exs. C, G, M.

Neurology Clerkship Director and a Professor of Neurology. Id. Dr. Naismith is also the Clinic Director of the John L. Trotter MS Center at Washington University and the Director of Clinical Trials in MS and Neuroimmunology. Id. at 2. He also holds various university and hospital appointments and committees. Id. at 2-3. His expertise includes MS, neuromyelitis optica, optic neuritis, and transverse myelitis. Resp. Ex. C at 2. He is also "familiar with [GBS] and ha[s] cared for many patients in [his] [more than] 16 years of practice." Id. Dr. Naismith has authored or co-authored over 100 publications. Resp. Ex. L at 10-18.

b. Opinion

Dr. Naismith agreed that Petitioner had GBS, as evidenced by her clinical presentation and nerve conduction studies. Tr. 167. The focus of his opinions was on causation.

i. Althen Prong One

While Dr. Naismith did not disagree with Petitioner's diagnosis of GBS, he disagreed that Petitioner set forth a reliable theory for how the Prevnar vaccine can cause GBS. Tr. 173. He opined that the Prevnar vaccine cannot cause GBS by preponderant evidence. Tr. 204. He based this on the fact that "there have been a number of epidemiologic studies . . . conducted, and they have not found there to be a relationship." Tr. 173-75. He opined that "case reports are difficult to interpret[] because they do not have the background rate incorporated into their analysis." Tr. 175. And he explained that GBS is mainly associated with the flu vaccine, with studies to support its association. Tr. 177. He did not believe that this association could be applied to "all vaccines." Id.

Further, he noted there is no mechanistic relationship because it is not generally accepted in the medical community that Prevnar 13 vaccine can caused GBS. Tr. 173-74. For example, Dr. Naismith explained that *Campylobacter* has been established as a cause of GBS established in the literature, which is not the case with Prevnar 13. Id. He also explained that because GBS has "an annual incidence of one to two per 100,000 patients," there will be "thousands of case[s] in the United States each year." Tr. 175. Meaning, "just by chance" some patients will get GBS after vaccination. Id.

Next, Dr. Naismith discussed case reports and medical literature. Regarding case reports, he noted they are "difficult to interpret" because the background rate of GBS is not "incorporated into their analysis." Tr. 175. He also pointed out there can be publication bias and case reports can be published in open access journals that have "minimal or no peer review." Tr. 175-76. Specific to the Ravishankar case report, Dr. Naismith disagreed that it provided evidence of a causal association between Prevnar 13 and GBS because there was no control and it did not account for the background rate of GBS. Tr. 191. He also noted that it was published in an open access journal where papers can be published for a fee. Id.

Dr. Naismith discussed four articles he cited in support of his opinions, starting with one authored by Souayah et al.[63] Tr. 178-81 (citing Resp. Ex. F, Tab 1). Souayah et al. used data from VAERS in 2004[64] for cases of GBS occurring within six weeks of vaccination. Resp. Ex. F, Tab 1 at 2. There were 54 cases of GBS reported after vaccination, with the highest number (23) occurring after the flu vaccine. Id. One case was reported after the pneumococcal polyvalent vaccine. Id. at 3.

The next article, by Stowe et al.,[65] examined cases of GBS with linked flu or pneumococcal vaccination records in the United Kingdom from 1990 to 2005.[66] Resp. Ex. F, Tab 2 at 2-4. There were 775 episodes of GBS occurring in 690 persons. Id. at 4. Of these, 69 had received at least one pneumococcal vaccine. Id. The focus of the study was on the flu vaccine; however, the authors found no increased risk of GBS after either the pneumococcal or flu vaccines. Id.

Dr. Naismith also discussed Baxter et al. Tr. 183-84 (citing Resp. Ex. E, Tab 3). This study examined 415 hospitalized cases of GBS from 1995 to 2006 from Kaiser facilities in Northern California,[67] and of the 415 cases, only 25 had received a vaccine, including PPSV, in the six weeks before onset of their illness. Resp. Ex. E, Tab 3 at 2, 5. The vaccine at issue here, Prevnar 13, was not studied.[68] Of the 25 patients identified as having GBS within six weeks of a vaccination, two had received the pneumococcal vaccine (PPSV23). Id. at 5. The authors found "no significant association" between vaccination and GBS. Id.

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[63] Nizar Souayah et al., Guillain-Barre Syndrome After Vaccination in United States: A Report from the CDC/FDA Vaccine Adverse Event Reporting System, 25 Vaccine 5253 (2007).

[64] Prevnar 13 was not administered in 2004. See About Pneumococcal Vaccines, Ctrs. for Disease Control & Prevention, https://www.cdc.gov/vaccines/vpd/pneumo/hcp/about-vaccine.html (last reviewed Sept. 11, 2024) (noting the FDA licensed Prevnar 13 in 2010).

[65] Julia Stowe et al., Investigation of the Temporal Association of Guillain-Barré Syndrome with Influenza Vaccine and Influenzalike Illness Using the United Kingdom General Practice Research Database, 169 Am. J. Epidemiology 382 (2009).

[66] It is not known when the pneumococcal vaccine was recommended for use and routinely administered in the United Kingdom.

[67] The first pneumococcal conjugate vaccine (PCV7) was not licensed for use until 2000. See About Pneumococcal Vaccines, Ctrs. for Disease Control & Prevention, https://www.cdc.gov/vaccines/vpd/pneumo/hcp/about-vaccine.html (last reviewed Sept. 11, 2024).

[68] See supra note 64. Although Prevnar 13 was not studied, PPSV23 contains serotypes 18C and 23F, which are also contained in Prevnar 13. See Pet. Ex. 32 at 11.

The last study discussed by Dr. Naismith, authored by Schwarz et al.,[69] compared the safety of the Prevnar 13 vaccine with the PPSV23 vaccine in 1,049 adults aged 68 or older from 2008 to 2009. Tr. 184-65; Resp. Ex. F, Tab 4 at 2-3. There were no serious adverse events with in the first month after receipt of Prevnar 13. Id. at 2. One case of GBS occurred 123 days after Prevnar 13 vaccination. Id. at 7.

Specific to the causal theory of molecular mimicry, Dr. Naismith cited Ang et al.,[70] who set forth four criteria to determine whether there is evidence to support molecular mimicry in the context of infections: (1) establishment of an epidemiological association between the infectious agent and the immune-mediated illness; (2) identification of T cells or antibodies directed against host target antigens demonstrated *in vivo* or *in vitro*; (3) identification of microbial mimic of target antigen; and (4) reproduction of the disease in an animal model. Tr. 186-89 (citing Resp. Ex. H at 2-4). Although Ang et al. recommends this approach for researching infectious causes of GBS, Dr. Naismith indicated he supported the use of the criteria in the context of vaccine causation "for establishing that there could be molecular mimicry." Tr. 186. He opined that none of the Ang et al. criteria have been met in this case. Tr. 186-89.

Moreover, Dr. Naismith observed that *S. pneumoniae* is not an infection that has been associated with GBS. Tr. 193 (citing Resp. Ex. E, Tab 1).[71] For support, he cited Jacobs et al., published in 1998, which identified the antecedent infections associated with GBS in 154 patients. Resp. Ex. E, Tab 1, at 4 tbl.1. Dr. Naismith also described his concerns with the Khatib et al. case report because "the neurologic symptoms seem[ed] to come before the infectious symptoms," causing him to question the temporal association between infection and onset of GBS. Tr. 194 (citing Pet. Ex. 14). He also expressed concern because diagnostic studies (lumbar puncture and NCS) were not done to confirm GBS. Id. (citing Pet. Ex. 14).

ii. Althen Prong Two

Dr. Naismith opined that Petitioner's Prevnar 13 vaccination did not cause her GBS. Tr. 167. Instead, he believed her URI symptoms were "notable" due to the strong association between infections and the development of GBS. Tr. 172. Therefore, while it was "difficult to be absolutely certain," he put infections "high on the list" of causes, and the most likely cause of Petitioner's GBS. Tr. 172-73, 206-07.

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[69] Tino F. Schwarz et al., Safety of a 13-Valent Pneumococcal Conjugate Vaccine in Elderly Adults Previously Immunized with a 23-Valent Pneumococcal Polysaccharide Vaccine: An Open-Label Trial, 3 World J. Vaccines 123 (2013).

[70] C. Wim Ang et al., The Guillain-Barré Syndrome: A True Case of Molecular Mimicry, 256 Trends Immunology 61 (2004).

[71] B.C. Jacobs et al, The Spectrum of Antecedent Infections in Guillain-Barré Syndrome: A Case-Control Study, 51 Neurology 1110 (1998).

In his first expert report, Dr. Naismith opined "[he] [did] not know why [] [P]etitioner developed GBS." Resp. Ex. C at 4. At the hearing, however, he opined that infection was the more likely cause of her GBS. Tr. 172-73, 206-07. During-cross examination, when asked to explain this difference in his opinions, Dr. Naismith explained that in his report, he was "referring to absolute medical certainly," while at the hearing, "we're talking about medical probability." Tr. 207.

Although Dr. Naismith opined that Petitioner's GBS was likely caused by an infection, he did not know whether it was viral or bacterial. Tr. 215. He stated he "[did not] think there's a way to know at this point. It could [have been] a viral infection." Id. Dr. Naismith agreed that if Petitioner had a bacterial infection, "it's possible" she would have had an elevated WBC count and fever. Tr. 215-16. He agreed that she did not have a fever. Tr. 217. He agreed that a protein component from a virus or bacteria could cause molecular mimicry. Tr. 221.

iii. Althen Prong Three

Petitioner received her vaccination on August 1, and Dr. Naismith opined that the onset of her GBS was August 18 or 19 when she developed neurological symptoms. Tr. 167. Prior to that, Petitioner had chills, felt feverish, fatigue, and malaise. Tr. 168.

4. Respondent's Expert, Dr. Kenneth H. Fife[72]

a. Background and Qualifications

Dr. Fife obtained his M.D. and Ph.D. from Johns Hopkins University School of Medicine. Resp. Ex. K at 1. He completed an internal medicine residency and an infectious disease fellowship. Tr. 252. Throughout his career, he held academic appointments at Indiana University School of Medicine as a Professor of Medicine, Professor of Microbiology and Immunology, and Professor of Pathology as well as hospital privileges at several hospitals in Indianapolis, Indiana. Resp. Ex. K at 2. Dr. Fife authored or co-authored over 150 publications throughout his career. Id. at 7-22.

Dr. Fife was board certified in internal medicine. Resp. Ex. K at 4. He was not board certified in infectious disease or immunology. Tr. 255, 290. At the time of the hearing, Dr. Fife had retired. Tr. 253.

b. Opinion

At the hearing, Dr. Fife opined that more likely than not, Petitioner's GBS was caused by a respiratory infection, not her Prevnar 13 vaccination. Tr. 259-60, 289. He testified that the Prevnar 13 vaccine did not cause her to develop GBS. Id. He noted that "[P]etitioner was most likely suffering from a respiratory infection that she complained of prior to developing

[72] Dr. Fife submitted one expert report and testified at the hearing. Tr. 250; Resp. Ex. A.

neurologic symptoms and these infections have been causally associated with the onset of GBS." Resp. Ex. A at 3.

Dr. Fife opined that Petitioner's GBS was post-infectious based on her signs and symptoms of chills, sweating, congestion, and sinus tenderness. Tr. 260-61 (citing Pet. Exs. 3-4). Although some of Petitioner's medical records identify a diagnosis of allergic sinusitis instead of infectious sinusitis, or fail to distinguish between the two, Dr. Fife believed her symptoms of night sweats and sinus tenderness pointed to infection. Id. Further, he noted that Petitioner was treated with an antibiotic (azithromycin), which is given for an infection. Tr. 262.

Petitioner's medical records document allergic sinusitis, however, Dr. Fife opined that Petitioner had an infectious sinusitis. Tr. 263. He cited a notation in Petitioner's medical records that stated she had a sinus infection. Id. (citing Pet. Ex. 2 at 31-33). He also noted that Petitioner had body aches and pains and chills, which were more typical of an infection than allergic sinusitis. Tr. 266. Dr. Fife conceded that Petitioner's ENT records indicated she had allergic sinusitis but that fact did not change his opinion that Petitioner's illness was infectious in nature. Tr. 267-68 (citing Pet. Ex. 19).

Dr. Fife testified that Petitioner had a "symptomatic fever" on August 15, 2015 because "she complained of feeling feverish." Tr. 297. He agreed, however, that Petitioner's temperature did not constitute a fever. Id. He reviewed Petitioner's medical records and agreed that there was no fever documented during the relevant period. Tr. 299-306.

Although Dr. Fife opined that Petitioner had an infection, he was unable to say whether the infection was viral or bacterial due to a lack of information. Tr. 262. He agreed that Petitioner did not have an elevated WBC, although it did increase mildly when she was admitted to the hospital. Id. However, that fact alone was not enough to indicate whether she had a viral or bacterial infection. Id.

With regard to the entry in Petitioner's medical records suggesting that she was diagnosed with bronchitis, Dr. Fife did not believe Petitioner had bronchitis. Tr. 262-63. Dr. Fife opined that the diagnosis of sinusitis and not bronchitis was more consistent with her physical examination due to the normal chest examination and normal chest X-ray. Tr. 263, 304-05. When he was asked on cross-examination if he had an opinion to a reasonable degree of medical probability as to whether Petitioner had bronchitis, Dr. Fife testified, "I don't think I can give an informed opinion." Tr. 294-95.

Dr. Fife agreed that various entries in Petitioner's medical records documented Petitioner had GBS from her Prevnar 13 vaccine, not from an infection. Tr. 295-96 (citing Pet. Ex. 19 at 1). And he agreed that Petitioner's medical records documented she had an allergic reaction to the Prevnar 13 vaccine. Tr. 302 (citing Pet. Ex. 3 at 4). When asked, he also agreed that Petitioner's PCP, Dr. Price, "clearly [thought] [Petitioner's] GBS was related to vaccination." Tr. 314 (citing Pet. Ex. 2 at 27).

Moving forward to Petitioner's causal theory based on molecular mimicry, Dr. Fife opined it was not a reputable theory because it "applies primarily to protein-related vaccines,"

whereas Prevnar 13 is made of polysaccharides with "no protein to cross-react with neuroproteins in the host." Tr. 268-69. He also opined that *S. pneumoniae* is not thought to be associated with GBS. Tr. 269-70. He cited Jacobs et al., stating that it "lists some of the infectious agents that have been associated with [GBS] and . . . supports[s] the notion that certain infections do precede [GBS]." Tr. 269. He testified that in Jacobs et al., *S. pneumoniae* was not one of the infections associated with GBS. Tr. 269-70 (citing Resp. Ex. E, Tab 1).

Jacobs et al. reported on a study of 154 patients with GBS in the Netherlands, which sought to identify antecedent infections associated with GBS and to determine whether GBS was "associated with specific antiganglioside antibodies." Resp. Ex. E, Tab 1 at 2-3. Based on serology studies, they found evidence of 11 infections in their GBS patients: *Campylobacter jejuni* ("*C. jejuni*") (32%), cytomegalovirus ("CMV") (13%), Epstein-Barr virus ("EBV") (10%), *Mycoplasma pneumoniae* ("*M. pneumoniae*") (5%), *Haemophilus influenzae* (1%), parainfluenza 1 virus (1%), flu A virus (1%), flu B virus (1%), adenovirus (1%), herpes simplex virus (1%), and varicella zoster virus (1%). Id. at 3. Only the first four were found more significantly frequent in the GBS patients when compared to controls, whereas the infections found in only 1% of patients were not found more frequently than in controls. Id. at 4. Only two infections, *C. jejuni* and CMV, were found to be related to specific antiganglioside antibodies. Id. at 1. Although the authors concluded that "certain infections are specifically related to GBS," they did not reach an opinion about other infections not identified in the study. Id. at 5. Moreover they did not conclude that only infections associated with antiganglioside antibodies were causally associated with GBS. Id. at 4-6.

There are several important points made in Jacobs et al. First, the authors discussed the difficultly discerning the identity of "GBS-related infections." Resp. Ex. E, Tab 1 at 2. The authors noted that research is based on "small" studies with "selected groups of GBS patients" not matched with appropriate controls, the studies lack serology confirmation of antecedent infections, and "the possible association among these infections, antiganglioside antibodies, and clinical presentation was not investigated" in most studies. Id.

Next, while they identified GBS-related infections, these infections (EBV or *M. pneumoniae*) "were not associated with the tested antiganglioside antibodies." Resp. Ex. E, Tab 1 at 4. Therefore, not all of the infections studied were associated with antiganglioside antibodies.

As expected, *C. jejuni* was found the be "the predominant cause of antecedent infection in GBS," as reported in other studies. Resp. Ex. E, Tab 1 at 6. Although the authors found *C. jejuni* occurred "more frequently" than the other infections identified, they postulated "one may argue that GBS is a postinfectious disease not related to specific infections," and that "the predominance of *C. jejuni* infections simply reflects the high frequency of this infection in the community." Id. And 13 (8%) of the GBS patients had an infection with more than one infectious agent (also reported in other studies). Id. Given this finding, the authors suggested that dual antigens may play a role in some GBS patients. Id.

After he discussed Jacobs et al., Dr. Fife turned to papers regarding vaccines causally related to GBS.[73] For example, Schonberger et al. described the association of GBS with the "swine flu vaccine" given in the United States in 1976-1977. Tr. 271-72 (citing Pet. Ex. 13). Out of 1,098 patients with GBS, 532 had received the A/New Jersey flu vaccine prior to onset of their GBS, and the epidemiologic evidence showed that many cases were related to vaccination. Pet. Ex. 13 at 2. Dr. Fife noted that the study showed "a strong association with the vaccine and the cases of GBS." Tr. 272.

Dr. Fife testified that he was not aware of any homology between Prevnar 13 and self-proteins that could cause GBS. Tr. 280, 283. He further opined that in molecular mimicry, protein antigens cross-react with human neural proteins, not polysaccharides. Tr. 283. Dr. Fife agreed there was a "carrier protein" in the Prevnar 13 vaccine that was "tetanus toxoid,"[74] which he opined "everybody gets multiple doses of, so its presumably not the cause of any GBS-type reaction." Tr. 284.

On cross-examination, Dr. Fife was asked a hypothetical question. See Tr. 292-93. He was asked to assume that he was responsible for monitoring for adverse events in a clinical trial of patients who were give Prevnar 13. Tr. 293. If a hypothetical patient developed the same signs and symptoms that Petitioner developed after vaccination, he was asked whether he would have reported her symptoms as an adverse event to Prevnar 13. Tr. 293. Dr. Fife answered, "Absolutely. Yes." Id. He would have rated the adverse events as a "possibly related" to vaccination. Id.

Dr. Fife also agreed that Petitioner's GBS had a temporal association with her vaccination. Tr. 331. Regarding his care of patients with GBS, he explained that while he had consulted on a few patients with GBS, he has never made the diagnosis of GBS, and would defer to a neurologist to do so. Tr. 322.

When asked about the mechanism by which a respiratory infection can cause GBS, Dr. Fife responded, "I don't know the mechanism." Tr. 331.

[73] Dr. Fife discussed studies other experts also discussed in detail. The undersigned has not repeated any discussion that would be duplicative. Dr. Fife did agree that Baxter et al. had "limited power to fully assess the risk of GBS following vaccination due to the rarity of outcome." Tr. 338 (citing Resp. Ex. E, Tab 3).

[74] The "protein carrier CRM_{197} . . . is a nontoxic variant of diphtheria toxin." Pet. Ex. 42 at 24 (package insert).

5. Respondent's Expert, Dr. J. Lindsay Whitton[75]

a. Background and Qualifications

Dr. Whitton received his B.Sc. in molecular biology, his M.B., Ch.B. in medicine, and his Ph.D. in herpesvirus transcription from the University of Glasgow in Scotland. Resp. Ex. O at 1. He held various professor positions since 1986. Id. He joined Scripps Research Institute in 1984 and remained there for many years. Id. He "studied (and published on) viral pathogenesis, and the immune responses to virus infections and to vaccines," and he has "published on both the adaptive and innate immune responses[] and on molecular mimicry." Resp. Ex. N at 1. Dr. Whitton is a member of various professional societies and editorial boards and has authored or co-authored approximately 200 publications. Resp. Ex. O at 1-15. Dr. Whitton does not hold a medical license, provide patient care, or diagnose or treat patients with GBS. Resp. Ex. N at 3.

b. Opinion

Dr. Whitton did not offer an opinion as to Petitioner's diagnosis or take a position on whether the diagnosis of GBS was appropriate. Resp. Ex. N at 3. His focus was on the question of whether the Prevnar 13 vaccine can cause GBS.[76] See Resp. Exs. N, P.

Dr. Whitton discussed the safety of Prevnar 13, explaining studies "have failed to find any increased risk of . . . GBS[] following pneumococcal vaccination." Resp. Ex. N at 7. Dr. Whitton reviewed studies by Baxter et al., Haber et al., and Tseng, et al. and noted that these studies did not support an increased risk of GBS following vaccination. Resp. Ex. N at 7 (citing Resp. Ex. E, Tab 3; Resp. Ex. E, Tab 4; Pet. Ex. 17).

A close review of these articles establish the limitations of the reported research. Baxter et al. studied 415 hospitalized patients with GBS from 1995 through 2006. Resp. Ex. E, Tab 3 at 2. Only 25 of these patients had received any vaccine within the six-week period prior to the onset of their GBS. Id. at 5. None received the Prevnar 13 vaccine,[77] and two received PPSV23. Id. The authors acknowledged that the study had "limited power to fully assess the risk of GBS following vaccination due to the rarity of the outcome." Id. at 8.

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[75] Dr. Whitton submitted two expert reports. Resp. Exs. N, P. He did not testify at the hearing.

[76] Dr. Whitton's criticisms of Dr. Steinman's expert opinions are far ranging. For the sake of brevity and clarity, the undersigned attempts to discuss the material points and omits discussion of criticism that is collateral to the central issues or that is characterized by Dr. Whitton as less important. Due to the length of Dr. Whitton's expert reports, some of his points have not been discussed here. However, the undersigned has reviewed Dr. Whitton's reports and the medical literature in its entirety and has taken all of this evidence into consideration in reaching her opinions.

[77] See supra note 64.

Haber et al. studied adverse events reported to VAERS in adults following the Prevnar 13 vaccine from June 2012 to December 2015. Resp. Ex. E, Tab 4 at 2. During that time, there were 2,976 reports, mostly related to injection site adverse events (pain, redness, and swelling). Id. There were 11 cases of GBS, and in ten of those patients, the Prevnar 13 vaccine was the only vaccine administered. Id. at 5. While the authors concluded that there was no disproportionate reporting for GBS, the reliance on VAERS data raised issues about the reliability of the results. Id. at 5-6. As noted by the authors, the limitations of VAERS "may include underreporting, varying quality of reports . . . , and the lack of an unvaccinated comparison group." Id. at 6.

The study by Tseng et al. only included adults 65 or older, and adverse events were compared between Prevnar 13 and PPSV23 instead of to a control group. Pet. Ex. 17 at 2. Twelve cases of GBS were found, four in the Prevnar 13 group, and 8 in the PPSV23 group. Id. at 7 tbl.3. The authors concluded there was "no significantly elevated risk" of GBS between the two groups. Id. at 8. It is difficult to discern whether the combined incidence of GBS after these vaccinations was higher than the background rate for GBS.

Second, Dr. Whitton opined that *S. pneumoniae*, which Prevnar 13 protects against, is not generally implicated as a cause of GBS. Resp. Ex. N at 10. He agreed that there are many infections associated with GBS, but *S. pneumoniae* is not one of them. Id. He concluded that since the organism does not trigger GBS, then the vaccine with the same antigens cannot do so. Id. at 11.

For molecular mimicry to occur, Dr. Whitton opined that three things must occur. Resp. Ex. N at 11-13. First, "[t]he vaccine material must induce an immune response." Id. at 12. Dr. Whitton stated that "one cannot assume that a response is made to every short sequence" and "if the allegedly-shared part of the vaccine material does not trigger an immune response, the chain of reasoning is broken." Id. As it relates to Dr. Steinman's theory, he explained that the question is whether the vaccine induces a response against "phosphoglycerol[] or to a few amino acids in the CRM_{197} carrier protein." Id. "If the vaccine material does trigger an immune response," then the immune response must recognize or cross-react with the "shared host material." Id. at 12-13. The third requirement is that the "cross-reactive immune response must be harmful" so as to induce disease. Id. at 13.

Dr. Whitton cited a paper from Rose and Mackay,[78] who wrote that "[t]here are[] [] no clear examples of a human disease caused by molecular mimicry." Resp. Ex. N at 14 (quoting Resp. Ex. N, Tab 24 at 1). He also quoted the 2012 Institute of Medicine ("IOM") Report,[79] which stated that "[w]hile molecular mimicry is a well-established mechanism in selected animal

[78] N.R. Rose & I.R. Mackay Molecular Mimicry: A Critical Look at Exemplary Instances in Human Diseases, 57 Cellular & Molecular Life Scis. 542 (2000). Dr. Whitton noted Dr. Rose was "an expert in immunology and sometimes referred to as 'the father of autoimmunity.'" Resp. Ex. N at 15.

[79] Inst. of Med., Evaluating Biological Mechanisms of Adverse Events, in Adverse Effects of Vaccines: Evidence and Causality 57 (Kathleen Stratton et al. eds., 2012).

models, its relevance to human autoimmune disease remains in most cases to be convincingly proven." Id. (quoting Resp. Ex. N, Tab 25 at 15). While Dr. Whitton agreed that molecular mimicry is "real," he believed it "cause[s] disease only rarely." Id. However, he agreed that GBS is an autoimmune disease, and that it is has been proposed that cases of GBS are triggered by molecular mimicry. Id. at 9.

After commenting on molecular mimicry generally, Dr. Whitton addressed the specific application of molecular mimicry in the theories offered by Dr. Steinman. According to Dr. Whitton, "the only reasonable established targets of autoimmune attack in some instances of GBS are gangliosides." Resp. Ex. N at 20. He cited a review article about GBS by Hughes et al.,[80] which does not mention the word "phospholipids" as an important target in GBS. Id. at 22 (citing Resp. Ex. N, Tab 26). He disagreed that papers cited and co-authored by Dr. Steinman indicating that phospholipids in the myelin sheath are targeted by antibodies are relevant because they are about MS, a disease of the central nervous system, and GBS involves the peripheral nervous system. Id. at 20-21 (citing Pet. Ex. 38;[81] Pet. Ex. 39). He also noted that another paper co-authored by Dr. Steinman proposed that the target of autoimmune attack in MS is GlialCAM, which is a protein, not a phospholipid. Id. at 21 (citing Pet. Ex. 56).

Dr. Whitton agreed that some strains of *S. pneumoniae* have polysaccharides chemically linked with a phosphoglycerol and that two of these are present in Prevnar 13 (18C and 23F). Resp. Ex. N at 16. But because phosphoglycerol is such a small molecule, he opined it is unlikely to trigger an immune response. Id. at 16-17. Dr. Whitton agreed that small molecules can be attached to larger ones, like carriers, so that the immune system can recognize it. Id. at 17. However, he disagreed with Dr. Steinman's "interpretation" of Bryson et al. Id. at 17-20 (citing Pet. Ex. 48). Dr. Whitton argued that the antibodies described by Bryson et al. do not recognize phosphoglcyerol alone, but "recognize it as [] part of an epitope in which the predominant components are the bacterial sugars (polysaccharides)." Id. at 18. He asserted that the Bryson et al. antibodies recognize the sugar and not the phosphoglycerol. Id. at 18-19.

Regarding Dr. Steinman's reference to Chang et al., Dr. Whitton disagreed that Chang et al. showed that phosphoglycerol linkage is necessary for the immunogenicity of the vaccine.[82] Resp. Ex. N at 26-28 (citing Pet. Ex. 45). Dr. Whitton also disagreed that Gilburd et al. supported the proposition that antibodies to phospholipids are seen in GBS because the authors

[80] Richard A.C. Hughes et al., Guillain-Barré Syndrome in the 100 Years Since its Description by Guillain, Barré and Strohl, 139 Brain 3041 (2016).

[81] Jennifer L. Kanter et al., Lipid Microarrays Identify Key Mediators of Autoimmune Brain Inflammation, 12 Nature Med. 138 (2006).

[82] Dr. Whitton suggested a different possibility for the "inclusion of phosphoglycerol as part of the epitope." Resp. Ex. N at 27. He also asserted that although "phosphoglycerol is used as a building block," when it is incorporated "into the much larger phospholipid, the phosphoglycerol is chemically altered . . . so that what is left is no longer phosphoglycerol" but only a very different remnant. Id. at 28. He also contended "there is no credible reason to suggest that this heavily[ ]modified remnant would retain the immunogenicity of the starting material." Id. at 31.

did not show that the antibodies were pathogenic, and instead noted that they were "probably produced as a result of the myelin damage rather than cause[d] the demyelination." Id. at 21 (citing Pet. Ex. 43 at 2). Next, he disagreed that Nakos et al. supported the idea that lipid antigens play a role in GBS. Id. at 31-32 (citing Pet. Ex. 44). He did not dispute the presence of antiphospholipid antibodies in some patients with GBS but stated that nowhere did the authors show that phosphoglycerol was "the target of the antibody response." Id. at 31. Further, according to Dr. Whitton, Nakos et al. did not demonstrate that there was any "relationship between these antibodies and the severity/outcome of GBS." Id. at 32. Regarding Ho et al., Dr. Whitton stated that it failed to show that antiphospholipid antibodies recognize phosphoglcyerol or its remnants. Id. at 32 (citing Pet. Ex. 39). And he noted that Ho et al. did not claim that phophoglycerol was the target of the antibodies. Id.

After addressing Dr. Steinman's phosphoglycerol theory,[83] Dr. Whitton turned to Petitioner's theory based on molecular mimicry between the CRM_{197} carrier protein in Prevnar 13 and a host protein Contactin-1.[84] Resp. Ex. N at 37-40. He maintained that when protein sequences are compared, short homologies will inevitably be found. Id. He opined that when "[c]omparing any host protein against any vaccine protein will inevitably reveal multiple short homologies." Id. at 39. Dr. Whitton criticized Dr. Steinman's use of a BLAST search and his proposed WEQ sequence on the basis that the E-value of 2.7 indicated that the sequence was "a chance finding[]." Id. at 40-47. Dr. Whitton opined that in order for a BLAST search to be immunologically relevant, the homology must fulfill the "Silvanovich criteria:" (1) the homology must be at least 80 amino acids long, (2) the homology must have 28 amino acids aligned, and (3) the "E-value must be lower than 3.9×10^{-7}." Id. at 44 (citing Resp. Ex. N, Tab 29; Resp. Ex. N, Tab 31). Because Dr. Steinman's BLAST results do not meet these criteria, Dr. Whitton believed the results are flawed. Id. at 45-48. Further, Dr. Whitton disagreed that Dr. Steinman's WEQ sequence had any significant similarity to Contactin-1. Id. at 53-54. For a number of reasons, Dr. Whitton concluded that the BLAST approach used by Dr. Steinman was not reliable. Id. at 40-48.

Next, although Dr. Whitton agreed Raju et al. showed that "some CD4+ T cells can respond to a longer [diphtheria toxin] peptide," he stated the paper did not reach any conclusions about antibody responses to the diphtheria toxin in CRM_{197}. Resp. Ex. N at 55. Therefore, Dr. Whitton believed Raju et al. was not relevant. Id.

In summary, Dr. Whitton opined that Dr. Steinman failed to provide evidence of molecular mimicry for his second theory based on the CRM_{197} protein in Prevnar 13 with Contactin-1.[85] Resp. Ex. N at 61-62. He noted that "Prevnar 13 has an excellent safety record" and he is "not aware of any reliable evidence that causally associates it with GBS." Id. at 62.

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[83] For a summary of Dr. Whitton's opinions about this theory, see Resp. Ex. N at 33-36.

[84] For a detailed discussion of Dr. Whitton's opinions about this second theory, see Resp. Ex. N at 37-61.

[85] For a complete summary, see Resp. Ex. N at 61-62.

III. DISCUSSION

A. Standards for Adjudication

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). Petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

In particular, a petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The received vaccine, however, need not be the predominant cause of the injury. Shyface, 165 F.3d at 1351. A petitioner who satisfies this burden is entitled to compensation unless Respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B). However, if a petitioner fails to establish a prima facie case, the burden does not shift. Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

"Regardless of whether the burden ever shifts to the [R]espondent, the special master may consider the evidence presented by the [R]espondent in determining whether the [P]etitioner has established a prima facie case." Flores v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 157, 162-63 (2014); see also Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the [P]etitioner's evidence on a requisite element of the [P]etitioner's case-in-chief."); Pafford, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

B. Factual Issues

Petitioner must prove, by a preponderance of the evidence, the factual circumstances surrounding her claim. § 13(a)(1)(A). To resolve factual issues, the special master must weigh the evidence presented, which may include contemporaneous medical records and testimony. See Burns v. Sec'y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (explaining that a special master must decide what weight to give evidence including oral testimony and contemporaneous medical records).

Contemporaneous medical records, "in general, warrant consideration as trustworthy evidence." Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). But see Kirby v. Sec'y of Health & Hum. Servs., 997 F.3d 1378, 1382 (Fed. Cir. 2021) (rejecting the presumption that "medical records are accurate and complete as to all the patient's physical conditions"); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 538 (2011) ("[T]he absence of a reference to a condition or circumstance is much less significant than a reference which negates the existence of the condition or circumstance." (quoting Murphy v. Sec'y of Health & Hum. Servs., 57 Cl. Ct. 726, 733 (1991), aff'd per curiam, 968 F.2d 1226 (Fed. Cir. 1992))), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013). The weight afforded to contemporaneous records is due to the fact that they "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium." Id. To overcome the presumptive accuracy of medical records, a petitioner may present testimony which is "consistent, clear, cogent, and compelling." Sanchez v. Sec'y of Health & Hum. Servs., No. 11-685V, 2013 WL 1880825, at *3 (Fed. Cl. Spec. Mstr. Apr. 10, 2013) (citing Blutstein v. Sec'y of Health & Hum. Servs., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)), mot. for rev. denied, 142 Fed. Cl. 247 (2019), vacated on other grounds & remanded, 809 F. App'x 843 (Fed. Cir. 2020).

There are situations in which compelling testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. Campbell v. Sec'y of Health & Hum. Servs., 69 Fed. Cl. 775, 779 (2006) ("[L]ike any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking."); Lowrie v. Sec'y of Health & Hum. Servs., No. 03-1585V, 2005 WL 6117475, at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) ("[W]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent." (quoting Murphy, 57 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); Bradley, 991 F.2d at 1575.

Despite the weight afforded to medical records, special masters are not bound rigidly by those records in determining onset of a petitioner's symptoms. Valenzuela v. Sec'y of Health & Hum. Servs., No. 90-1002V, 1991 WL 182241, at *3 (Fed. Cl. Spec. Mstr. Aug. 30, 1991); see also Eng v. Sec'y of Health & Hum. Servs., No. 90-1754V, 1994 WL 67704, at *3 (Fed. Cl. Spec. Mstr. Feb. 18, 1994) (Section 13(b)(2) "must be construed so as to give effect also to §

13(b)(1) which directs the special master or court to consider the medical records (reports, diagnosis, conclusions, medical judgment, test reports, etc.), but does not require the special master or court to be bound by them").

C. Causation

To receive compensation through the Program, Petitioner must prove either (1) that she suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that she received, or (2) that she suffered an injury that was actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); Capizzano, 440 F.3d at 1319-20. Petitioner must show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface, 165 F.3d at 1352-53).

Because Petitioner does not allege she suffered a Table Injury, she must prove a vaccine she received actually caused her injury. To do so, Petitioner must establish, by preponderant evidence: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278.

The causation theory must relate to the injury alleged. Petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on her assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether Petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The special master must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in Petitioner's favor when the evidence weighs in her favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in Petitioner's favor).

Testimony that merely expresses the possibility—not the probability—is insufficient, by itself, to substantiate a claim that such an injury occurred. See Waterman v. Sec'y of Health & Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying Petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard). The Federal Circuit has made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). While certainty is

by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322; see also de Bazan, 539 F.3d at 1351.

IV. ANALYSIS

A. Factual Dispute

The factual issue in dispute is whether Petitioner's symptoms of August 15, 2015 were "allergic in nature or consistent with an [URI]." Joint Submission at 2. The undersigned finds there is preponderant evidence that Petitioner's symptoms represented an allergic sinusitis and there is not preponderant evidence of a respiratory infection. These findings are based on facts set forth in the medical records, the treating health care providers' diagnoses on August 15 as well as on subsequent visits, and the opinions of Petitioner's expert, Dr. Napoli.

On August 15, the records show that Petitioner did not have fever, ear discharge or pain, sore throat, shortness of breath, or wheezing. Her physical examination that day documented that she was afebrile, in no distress, her ear canals had no redness, she had no respiratory distress, and no cervical adenopathy. She did have a runny nose, but there was no nasal mucosal edema (swelling). Petitioner's chest X-ray was normal. And her WBC count was also normal. Petitioner was diagnosed with cough, malaise, fatigue, and sinusitis. An antibiotic (azithromycin) and steroids were prescribed.

The experts disputed whether Petitioner's sinusitis was allergic or infectious. The nurse practitioner who saw Petitioner on August 15 did not specify whether her sinusitis was allergic or infectious. The nurse did order an antibiotic, but that alone is not determinative. There are other facts that weigh against finding Petitioner had an infection including the absence of fever, ear pain or discharge, sore throat, shortness of breath or wheezing, and cervical adenopathy that would indicate swelling of the lymph nodes, as well as a normal chest X-ray and WBC count.

Further, Petitioner's expert neurologist, Dr. Napoli, noted that health care providers often order antibiotics "to be on the safe side" and to ensure that Petitioner did not develop a bacterial infection on top of her allergic condition. Tr. 70. Dr. Napoli opined that Petitioner's presentation on August 15 was not consistent with infection for the reasons identified above. See Tr. 70-76.

Moreover, Petitioner's subsequent records do not support a finding that Petitioner had an infection on August 15. Two days later, on August 17, Petitioner saw her PCP, Dr. Price, and he did not diagnose an infection. Instead, his diagnosis was "[a]llergic sinusitis." Pet. Ex. 2 at 32. He did not prescribe antibiotics or consider either a bacterial or viral infection. On August 19, two days following her visit to Dr. Price, Petitioner went to the ER at Doctors Hospital for weakness, fatigue, and falls. She had no fever. She was not diagnosed with infection.

Petitioner returned to the ER at Doctors Hospital on August 21, again with weakness, and was admitted. She was seen by Dr. Bathina, who wrote a detailed history and documented a review of systems and physical examination. Dr. Bathina opined Petitioner "[did] not have any

source of infection and she [was] not going to be started on any IV antibiotics." Pet. Ex. 4 at 1109.

While Petitioner reported to her providers that she had a URI and/or bronchitis, these two entries appear to be statements made by Petitioner when she was reporting her history. Petitioner's records, however, do not document that she was diagnosed with bronchitis or URI on any of these dates. Therefore, the origin of these statements in not clear. Regardless of these entries, the fact remains that Petitioner was not given a diagnosis of bronchitis or URI.

Respondent's infectious disease expert, Dr. Fife, opined that Petitioner had an infection based on her night sweats, chills, congestion, and sinus tenderness. He also noted that she was prescribed an antibiotic. However, he was unable to state whether she had a viral or bacterial infection. He agreed that she did not have an elevated WBC count. Overall, the undersigned did not find Dr. Fife's opinion persuasive, as compared with the records and diagnoses documented by the treating health care providers.

In summary, Petitioner was seen by four different health care providers on four different occasions over the period of a week—August 15, 17, 19, and 21. None of them documented that she had an infection or diagnosed her with an infection.

Opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326. Additionally, medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528.

For all of the reasons described above, the undersigned finds there is preponderant evidence that Petitioner's symptoms represented an allergic sinusitis, not a respiratory infection.

B. Causation

1. Althen Prong One

Under Althen prong one, Petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu, 569 F.3d at 1375; Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 257 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If Petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better

than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

The undersigned finds Petitioner has provided, by preponderant evidence, a sound and reliable theory by which the Prevnar 13 vaccine can cause GBS, and therefore, Petitioner has satisfied the first Althen prong. There are several reasons for this finding. Molecular mimicry has long been invoked as the causal mechanism for GBS and it is a sound and reliable theory in this context. Dr. Steinman posits two theories for how the Prevnar 13 vaccine can cause GBS via molecular mimicry and the foundation for these theories are based on sound and reliable evidence. Second, Respondent's experts evaluate these theories using criteria that exceed the legal standards set forth in the Vaccine Act. And third, the proposed causal mechanisms have been offered in past cases and accepted as sound and reliable.

Molecular mimicry has been accepted as a sound and reliable theory in many demyelinating conditions, including GBS, in the Vaccine Program, forming the basis for petitioners to be entitled to compensation. See, e.g., Conte v. Sec'y of Health & Hum. Servs., No. 17-403V, 2020 WL 5743696, at *57 (Fed. Cl. Spec. Mstr. July 27, 2020) (noting the theory of molecular mimicry in a GBS case is "well-established and well-settled in the Vaccine Program"); Barone v. Sec'y of Health & Hum. Servs., No. 11-707V, 2014 WL 6834557, at *8-9 (Fed. Cl. Spec. Mstr. Nov. 12, 2014) (noting molecular mimicry "has been accepted in other Program cases as a reliable medical explanation for how various autoimmune conditions could develop after the receipt of different kinds of vaccinations"). Petitioners have also been found to be entitled to compensation for GBS caused by various vaccines. See, e.g., Salmins v. Sec'y of Health & Hum. Servs., No. 11-140V, 2014 WL 1569478, at *14 (Fed. Cl. Spec. Mstr. Mar. 31, 2014) (finding HPV vaccine can cause GBS); Peugh v. Sec'y of Health and Hum. Servs., No. 99-638V, 2007 WL 1531666, at *17 (Fed. Cl. Spec. Mstr. May 8, 2007) (finding hepatitis B vaccine can GBS); Whitener v. Sec'y of Health & Hum. Servs., No. 06-0477V, 2009 WL 3007380, at *20 (Fed. Cl. Spec. Mstr. Sept. 2, 2009) (finding meningococcal vaccine can cause GBS); Koller v. Sec'y of Health & Hum. Servs., No. 16-439V, 2021 WL 5027947, at *7-20 (Fed. Cl. Spec. Mstr. Oct. 8, 2021) (finding Prevnar 13 can cause GBS); Mohamad v. Sec'y of Health & Hum. Servs., No. 16-1075V, 2022 WL 711604, at *9-18 (Fed. Cl. Spec. Mstr. Jan. 27, 2022) (finding tetanus-diphtheria-acellular pertussis vaccine can cause GBS); J.G. v. Sec'y of Health & Hum. Servs., No. 20-664V, 2023 WL 2752634, at *29-32 (Fed. Cl. Spec. Mstr. Feb. 13, 2023) (finding hepatitis A vaccine can cause GBS). And even in cases where there has been no evidence of homology, molecular mimicry has been accepted as a theory of causation. See, e.g., Salmins, 2014 WL 1569478, at *14.

Dr. Whitton rejects Dr. Steinman's theory based on molecular mimicry in part because it does not involve anti-ganglioside antibodies. However, this viewpoint is not supported by medical literature and studies which show that not all patients with GBS have anti-ganglioside antibodies. For example, the results reported in Jacobs et al. argues against a conclusion that molecular mimicry must involve gangliosides since the study identified multiple antecedent infectious agents, both bacterial and viral, but antibodies to gangliosides were only identified in two, *C. jejuni* and CMV. See Resp. Ex. E, Tab 1 at 2. The authors concluded that "[a] remarkable diversity of infectious agents has been reported in patients with GBS . . . . The variety of reported infectious agents in GBS may therefore underlie the immunologic and clinical

heterogeneity in GBS." Id. Where there is "remarkable diversity" in the etiology of infectious agents, and where the scientists who study molecular mimicry in the context of GBS suggest there is "immunologic and clinical heterogeneity," it is not reasonable to assume there is only one host target susceptible to immune attack without studies that support such a conclusion. See Bartoszek v. Sec'y of Health & Hum. Servs., No. 17-1254V, 2024 WL 4263604, at *19-22, *19 n.16 (Fed. Cl. Spec. Mstr. Aug. 27, 2024);

The second reason the undersigned finds Petitioner's causal theories sound and reliable is that they satisfied the legal standards articulated in the Vaccine Act. In contrast, both of Respondent's experts articulate standards which exceed those required by the Act.

Dr. Naismith evaluates the causal theory here based on the four criteria discussed in Ang et al.: (1) establishment of an epidemiological association between the infectious agent and the immune-mediated illness; (2) identification of T cells or antibodies directed against host target antigens demonstrated *in vivo* or *in vitro*; (3) identification of microbial mimic of target antigen; and (4) reproduction of the disease in an animal model.

Dr. Whitton has three criteria. The vaccine material must induce an immune response, the immune response must recognize or cross react with the shared host material, and the response must be harmful. These are like the IOM criteria required to establish whether a vaccine can cause GBS via molecular mimicry. The criteria include (1) "a susceptible host" (genetically and via host immune responses), (2) "exposure to an exogenous agent which expresses antigens that are immunologically similar to self-antigen(s), and (3) a host immune response" that causes disease. Resp. Ex. N, Tab 25 at 14. Further, there must be evidence of an "in vivo pathogenic autoimmune attack" and demonstration of the pathogenic mechanisms "in a biologically relevant tissue site." Id. at 15.

Given the state of current scientific knowledge, it would be impossible for a Petitioner to satisfy the criteria proposed by Dr. Naismith or Dr. Whitton. Further, fulfilment of these criteria would require scientific certainty, which is a bar too high. See Knudsen, 35 F.3d at 549 (explaining that "to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program").

Dr. Steinman identified components of the vaccine that could initiate development of antibodies that could cross-react with epitopes on peripheral nerve myelin. He has identified components of the Prevnar 13 vaccine that could trigger a human antibody response.

Regarding Petitioner's theory based on phosphoglycerol in serotypes 18C and 23F in the vaccine, Dr. Steinman produced papers to show that in MS, myelin phospholipids are targeted by an immune response. He also showed that myelin is comprised of phospholipids, and that phospholipids can serve as autoantigens in autoimmune disorders. He showed patients with GBS have autoantibodies to phospholipids. In the Gilburd et al. study, the autoantibodies were thought to be due to myelin destruction. However, in Nakos et al., the researchers had a different view. They suggested that anti-phospholipids either "play a role in pathogenesis of the polyneuropathy or represent a part of a more extensive immunoreaction that takes place in []

GBS." Pet. Ex. 44 at 6. In summary, there is sound support from reputable medical studies for each foundational aspect of Dr. Steinman's phosphoglycerol theory.

There is also evidence to support Dr. Steinman's second theory based on CRM_{197} and Contactin-1. Dr. Steinman identified sequences of shared homology between the proteins in the vaccine and those in Contactin-1. He also explained how an immune response to Contactin-1 could cause GBS.

Additionally, the causal theory proffered by Dr. Steinman here has previously been accepted as sound and reliable in at least 10 other Prevnar 13 cases, decided by different special masters, including the undersigned. See, e.g., Bartoszek, 2024 WL 4263604, at *17-22; Byrd v. Sec'y of Health & Hum. Servs., No. 20-1476V, 2024 WL 2003061, at *21-26 (Fed. Cl. Spec. Mstr. July 8, 2024); Cooper v. Sec'y of Health & Hum. Servs., No. 18-1885V, 2024 WL 1522331, at *14-18 (Fed. Cl. Spec. Mstr. Mar. 12, 2024); Anderson ex rel. Meyer v. Sec'y of Health & Hum. Servs., No. 18-484V, 2024 WL 557052, at *30-32 (Fed. Cl. Spec. Mstr. Jan. 17, 2024); Parker v. Sec'y of Health & Hum. Servs., No. 20-411V, 2023 WL 9261248, at *20-22 (Fed. Cl. Spec. Mstr. Dec. 20, 2023); Sprenger v. Sec'y of Health & Hum. Servs., No. 18-279V, 2023 WL 8543435, at *18-20 (Fed. Cl. Spec. Mstr. Nov. 14, 2023); Gross v. Sec'y of Health & Hum. Servs., No. 17-1075V, 2022 WL 9669651 (Fed. Cl. Spec. Mstr. Sept. 22, 2022); Maloney v. Sec'y of Health & Hum. Servs., No. 19-1713V, 2022 WL 1074087 (Fed. Cl. Spec. Mstr. Mar. 17, 2022); Pierson v. Sec'y of Health & Hum. Servs., No. 17-1136V, 2022 WL 322836, at *27-31 (Fed. Cl. Spec. Mstr. Jan. 19, 2022); Koller, 2021 WL 5027947, at *18. While prior decisions are not binding on the undersigned, they can be considered by the undersigned in forming her opinions. See Hanlon v. Sec'y of Health & Hum. Servs., 40 Fed. Cl. 625, 630 (1998), aff'd, 191 F.3d 1344 (Fed. Cir. 1999); Boatmon, 941 F.3d at 1358. The undersigned agrees with the reasoning offered by her colleagues in these other cases, and for many of the same reasons finds the Petitioner's theory here sound and reliable and proven by preponderant evidence.

The undersigned recognizes that there is not uniformity between the special masters in decisions addressing the Prevnar 13 vaccine and GBS. In some of these cases, there are factual issues that affected the outcome. See, e.g., McConnell v. Sec'y of Health & Hum. Servs., No. 18-1051V, 2022 WL 4008238, at *5-11 (Fed. Cl. Spec. Mstr. Aug. 19, 2022) (noting disputes with diagnosis and onset, but ultimately finding Petitioner did not provide preponderant evidence in support of Althen prongs). And in others, the special master did not accept Petitioner's theory, finding Petitioner did not provide preponderant evidence in support of Althen prong one. See, e.g., Deshler v. Sec'y of Health & Hum. Servs., No. 16-1070V, 2020 WL 4593162, at *19-21 (Fed. Cl. Spec. Mstr. July 1, 2020); Trollinger v. Sec'y of Health & Hum. Servs., No. 16-473V, 2023 WL 2521912, at *27-30 (Fed. Cl. Spec. Mstr. Feb. 17, 2023), mot. for rev. denied, 167 Fed. Cl. 127; Bielak v. Sec'y of Health & Hum. Servs., No. 18-761V, 2023 WL 35509, at *33-37 (Fed. Cl. Spec. Mstr. Jan. 3, 2023); Gamboa-Avila v. Sec'y of Health & Hum. Servs., No. 18-925V, 2023 WL 6536207, at *26-32 (Fed. Cl. Spec. Mstr. Sept. 11, 2023), mot. for rev. denied, 170 Fed. Cl. 441 (2024), appeal docketed, No. 2024-1765 (Fed. Cir. May 1, 2024); Morrison v. Sec'y of Health & Hum. Servs., No. 18-386V, 2024 WL 3738934, at *17-24 (Fed. Cl. Spec. Mstr. July 18, 2024). The undersigned acknowledges these cases but also notes that the decisions of other special masters or Court of Federal Claims' judges are not binding on special masters. Boatmon, 941 F.3d at 1358; Hanlon, 40 Fed. Cl. at 630.

For these reasons, the undersigned finds that Petitioner has proven by preponderant evidence a sound and reliable causal theory establishing that the Prevnar 13 vaccine can cause GBS, satisfying Althen prong one.

2. Althen Prong Two

Under Althen prong two, Petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "Petitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (internal citations omitted).

A petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

There are three reasons why the undersigned finds preponderant evidence of a logical sequence of cause and effect establishing that the Prevnar 13 vaccination administered to Petitioner on August 1, 2015 was the cause of her GBS. First, Petitioner was appropriately diagnosed with GBS, and Petitioner has proffered a sound and reliable mechanism of vaccine causation.

Second, the undersigned finds that preponderant evidence does not support an alternative cause (URI) was the cause of Petitioner's GBS for the reasons described above. To summarize, Petitioner's medical records from August 15 weigh against finding Petitioner had an infection. Petitioner did not have a fever, ear pain or discharge, sore throat, shortness of breath or wheezing, or cervical adenopathy, nor was she diagnosed with an URI. She had a normal chest X-ray and WBC count. And although she was prescribed an antibiotic, the undersigned does not find that fact alone determinative. Additionally, Petitioner's subsequent records in August 2015 continued to document no signs or symptoms consistent with an infection. See, e.g., Pet. Ex. 4 at 1109 (Dr. Bathina documenting on August 21, 2015 that Petitioner "[did] not have any source of infection and she [was] not going to be started on any IV antibiotics"). Overall, Petitioner was seen by numerous health care providers on four different occasions from August 15 to August 21, 2015, and none documented Petitioner had an infection or diagnosed her with an infection.

The third reason for finding that Petitioner has proven prong two is based on the statements and opinions by Petitioner's treating physicians. Neurologist Dr. Wolf diagnosed Petitioner with GBS and noted Prevnar 13 as a "[p]otential antigenic trigger." Pet. Ex. 4 at 1115. Triggers were documented throughout Petitioner's hospital records. See, e.g., id. at 1123, 1130, 1135, 1139, 1149, 1154, 1249. Her discharge summary noted her GBS was "thought to be due to viral illness or recent pneumococcal vaccination." Id. at 1092. Dr. Price's records document "[GBS] following vaccination" or "due to vaccination" many times. Pet. Ex. 2 at 2, 4, 7-9, 11,

13-23, 25, 27-28, 30. His records also continually list GBS post-Prevnar 13 vaccine as an allergy. See id. at 2, 7, 10, 14, 17, 20, 23, 26, 29.

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. While the medical records and opinions of treating physicians must be considered, they are not binding on the special master. § 13(b)(1)(B) (specifically stating that the "diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court").

In conclusion, the undersigned finds that Petitioner has proven by preponderant evidence a logical sequence of cause and effect establishing that the Prevnar 13 vaccination caused Petitioner's GBS. Thus, Petitioner has satisfied the second Althen prong.

3. Althen Prong Three

Althen prong three requires Petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That phrase has been defined as a "medically acceptable temporal relationship." Id. A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen prong one). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1579, 1243 (Fed. Cir. 2014); Shapiro, 101 Fed. Cl. at 542.

The parties stipulate that Petitioner received her Prevnar 13 vaccination on August 1, 2015. The records show that when Petitioner was evaluated on August 21 at Doctors Hospital, she reported that the onset of her weakness was August 18. This report is consistent with her complaints of weakness, fatigue, and falls when she presented earlier, on August 19.

The experts' opinions regarding onset range from two to three weeks after vaccination. Dr. Napoli opined that Petitioner's onset manifested as back pain, malaise, fatigue, weakness, and gait problems that occurred approximately two to three weeks after vaccination. Dr. Steinman opined that onset occurred approximately three weeks after vaccination. Respondent's expert, Dr. Naismith opined that onset was August 18 or 19, when she had neurological symptoms. Dr. Fife agreed that Petitioner's onset was temporally associated with her vaccination, and Dr. Whitton did not refute a temporal association.

The undersigned finds that onset was August 18 or 19 when Petitioner had weakness, approximately 18 days after vaccination, as demonstrated by her medical records. Respondent's experts do not rebut the onset time frame or otherwise dispute that there was a temporal

association between the vaccination and onset of GBS consistent with the theory of molecular mimicry.

This time frame from vaccination to the initial manifestation of symptoms is appropriate given the theory of molecular mimicry, as demonstrated in Haber et al., which reported 11 cases of GBS following a Prevnar 13 vaccine, with a median onset interval of nine days and a range of two to 42 days. This temporal association is also consistent with the onset period of three to 42 days as set forth in the Vaccine Injury Table for GBS following flu vaccination. 42 C.F.R. § 100.3(a)(XIV)(D).

Further, this time frame has been acknowledged as appropriate in other Vaccine Program cases in which molecular mimicry has been proffered as the causal mechanism. See, e.g., Bartoszek, 2024 WL 4263604, at *24-25 (finding a GBS onset of 22 days, or approximately three weeks, post-Prevnar 13 vaccination to be medically acceptable); Sprenger, 2023 WL 8543435, at *22 (finding a GBS onset of approximately two weeks after Prevnar 13 vaccination to be appropriate); Gross, 2022 WL 9669651, at *38-39 (finding a GBS onset of 13 days after Prevnar 13 vaccination to be appropriate); Koller, 2021 WL 5027947, at *23 (finding a GBS onset of 12 days after Prevnar 13 vaccination to be "within the medically accepted timeframe consistent with [P]etitioner's theory of molecular mimicry [and] that has been accepted in other Vaccine Program cases"); see also Barone, 2014 WL 6834557, at *13 ("[S]pecial masters have never gone beyond a two-month (meaning eight week) interval in holding that a vaccination caused a demyelinating illness.").

Therefore, undersigned finds that Petitioner has met her burden of proof as to Althen prong three.

V. CONCLUSION

Based on the record, and for the reasons discussed above, the undersigned finds there is preponderant evidence to satisfy all three Althen prongs and to establish that Petitioner's Prevnar 13 vaccination caused her to develop GBS. Thus, the undersigned finds that Petitioner is entitled to compensation. A separate damages order will issue.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master